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PASSWORD:

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NEWS 5 DEC 14 2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
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NEWS 7 DEC 21 IPC search and display fields enhanced in CA/CAPplus with the
IPC reform
NEWS 8 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
USPAT2
NEWS 9 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 10 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
INPADOC
NEWS 11 JAN 17 Pre-1988 INPI data added to MARPAT
NEWS 12 JAN 17 IPC 8 in the WPI family of databases including WPIFV
NEWS 13 JAN 30 Saved answer limit increased
NEWS 14 JAN 31 Monthly current-awareness alert (SDI) frequency
added to TULSA

NEWS EXPRESS JANUARY 03 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
<http://download.cas.org/express/v8.0-Discover/>

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* * * * * STN Columbus * * * * *

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 1.05 | 1.05 |

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STRUCTURE FILE UPDATES: 6 FEB 2006 HIGHEST RN 873652-66-5
DICTIONARY FILE UPDATES: 6 FEB 2006 HIGHEST RN 873652-66-5

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```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
*
*****
```

Structure search iteration limits have been increased. See HELP SLIMITS
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REGISTRY includes numerically searchable data for experimental and
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=>

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L1 STRUCTURE UPLOADED

=> s sss full 11

GENERIC GROUP NOT VALID HERE

Generic groups may not be used in these circumstances:

1. Any generic group node (e.g., Hy) in a ring.
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=>

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L2 STRUCTURE UPLOADED

=> s sss full 12

FULL SEARCH INITIATED 14:43:18 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 36137 TO ITERATE

100.0% PROCESSED 36137 ITERATIONS
SEARCH TIME: 00.00.01

368 ANSWERS

L3 368 SEA SSS FUL L2

=> file caplus uspatful

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

170.46

171.51

FILE 'CAPLUS' ENTERED AT 14:43:36 ON 07 FEB 2006

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE 'USPATFULL' ENTERED AT 14:43:36 ON 07 FEB 2006

CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s l3

L4 113 L3

=> s l4 and (depression or antidepressant? or mood or mania or manic? or sadness)

L5 23 L4 AND (DEPRESSION OR ANTIDEPRESSANT? OR MOOD OR MANIA OR MANIC?
OR SADNESS)

=> dup rem l4

PROCESSING COMPLETED FOR L4

L6 105 DUP REM L4 (8 DUPLICATES REMOVED)

=> dup rem l5

PROCESSING COMPLETED FOR L5

L7 22 DUP REM L5 (1 DUPLICATE REMOVED)

=> d ibib abs hitstru 1-22

'HITSTRU' IS NOT A VALID FORMAT

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in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> focus

PROCESSING COMPLETED FOR L7

L8 22 FOCUS L7 1-

=> d ibib abs it 1-22

L8 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1976:543152 CAPLUS

DOCUMENT NUMBER: 85:143152

TITLE: 7,7-Diphenylhexahydro-1,4-oxazepines

INVENTOR(S): Bowman, Robert M.

PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.

SOURCE: Ger. Offen., 65 pp.

CODEN: GWXXBX

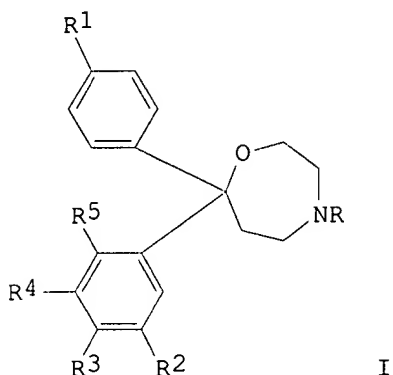
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| DE 2552196 | A1 | 19760526 | DE 1975-2552196 | 19751121 |
| US 3988448 | A | 19761026 | US 1974-526758 | 19741125 |
| ZA 7506191 | A | 19760929 | ZA 1975-6191 | 19750930 |
| DK 7505052 | A | 19760526 | DK 1975-5052 | 19751110 |
| FI 7503182 | A | 19760526 | FI 1975-3182 | 19751112 |
| SE 7512746 | A | 19760526 | SE 1975-12746 | 19751113 |
| NL 7513530 | A | 19760528 | NL 1975-13530 | 19751119 |
| NO 7503927 | A | 19760526 | NO 1975-3927 | 19751121 |
| BE 835855 | A1 | 19760524 | BE 1975-162108 | 19751124 |
| ZA 7507368 | A | 19761124 | ZA 1975-7368 | 19751124 |



AB Hexahydrooxazepines I (R = PhCH₂, H, Me, allyl, HC.tplbond.CCH₂, cyclopropylmethyl, furfuryl, EtCOCH₂, cyanoethyl, etc.; R₁ = H F; R₂ = H, MeO, Cl, F; R₃ = H, MeO, F, OH; R₄ = H, F, MeO; R₅ = H, MeO) and(or) their HCl or cyclohexylsulfamic acid salts (40 compds.), useful as **antidepressants** at 20 mg/kg/day in rats or mice, were prepared by 6 methods. Thus, e.g., I (R = PhCH₂, R₁-R₅ = H) (II) was prepared in 7 steps from MeCN and Ph₂CO via HOCPh₂CH₂CH₂NHBz and the 3-oxoanalog of II. HOCPh₂CH₂CN and ICH₂CH(OEt)₂ gave NCCH₂CPh₂OCH₂CH(OEt)₂ which was reduced and cyclized by hydrogenation to give I (R-R₅ = H) which was alkylated to give I (R = allyl, CH₂CH₂OH, furfuryl, HC.tplbond.CCH₂, cyclopropylmethyl, etc.).

IT **Antidepressants**

(hexahydrodiphenyloxazepines)

IT 4023-34-1

RL: RCT (Reactant); RACT (Reactant or reagent)
 (acylation of (aminodiphenylpropoxy)acetaldehyde diethyl acetal)

IT 79-04-9

RL: RCT (Reactant); RACT (Reactant or reagent)
 (acylation of benzylhydroxydiphenylpropylamines by)

IT 60163-68-0 60163-69-1 60163-70-4 60163-71-5 60280-67-3

RL: RCT (Reactant); RACT (Reactant or reagent)
 (alkylation of)

IT 75-21-8, reactions 106-95-6 107-13-1, reactions 107-14-2 3874-54-2

RL: RCT (Reactant); RACT (Reactant or reagent)
 (alkylation of diphenylhexahydrooxazepines by)

IT 98-88-4

RL: RCT (Reactant); RACT (Reactant or reagent)
 (benzoylation of hydroxydiphenylpropylamines by)

IT 60163-58-8

RL: RCT (Reactant); RACT (Reactant or reagent)
 (condensation with formaldehyde and reduction)

IT 100-52-7, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
 (condensation with hydroxydiphenylpropylamine)

IT 60163-67-9

RL: RCT (Reactant); RACT (Reactant or reagent)
 (cyclization of)

IT 60163-40-8P 60163-41-9P 60163-42-0P 60163-43-1P 60163-44-2P

60163-46-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and N-chloroacetylation of)

IT 60163-65-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and allylation of)

IT 50775-34-3P 60163-33-9P 60163-34-0P 60163-35-1P 60163-36-2P
60163-60-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and benzylation of)

IT 60163-61-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and chloroacetylation of)

IT 60162-88-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and chloroformylation of)

IT 60163-47-5P 60163-48-6P 60163-49-7P 60163-50-0P 60163-51-1P
60163-52-2P 60163-62-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and cyclization of)

IT 60163-45-3P 60163-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenolysis of)

IT 3531-23-5P 4320-44-9P 60163-56-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reactions of)

IT 50775-33-2P 60162-89-2P 60162-90-5P 60162-91-6P 60162-92-7P
60162-93-8P 60163-16-8P 60163-21-5P 60163-29-3P 60163-30-6P
60163-31-7P 60163-32-8P 60163-37-3P **60163-38-4P**
60163-39-5P 60163-53-3P 60163-55-5P 60163-59-9P 60163-60-2P
60163-63-5P 60181-44-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reduction of)

IT 60162-87-0P 60162-89-2P 60162-90-5P 60162-91-6P 60162-92-7P
60162-93-8P 60162-94-9P 60162-95-0P 60162-96-1P 60162-97-2P
60162-98-3P 60162-99-4P 60163-00-0P 60163-01-1P 60163-02-2P
60163-03-3P 60163-04-4P 60163-05-5P 60163-06-6P 60163-08-8P
60163-09-9P 60163-10-2P 60163-11-3P 60163-12-4P 60163-13-5P
60163-14-6P 60163-15-7P 60163-17-9P 60163-18-0P 60163-19-1P
60163-20-4P 60163-22-6P 60163-23-7P 60163-25-9P 60163-26-0P
60163-27-1P 60163-28-2P 60163-57-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 345-92-6 1016-78-0 2553-04-0 6136-67-0 54589-41-2 55363-58-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with acetonitrile)

IT 541-41-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzyldiphenylhexahydrooxazepine)

IT 51806-20-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxydiphenylpropionitriles)

IT 60163-54-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactions of)

IT 60163-66-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)

IT 119-61-9, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(with acetonitrile)

IT 75-05-8, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(with benzophenones)

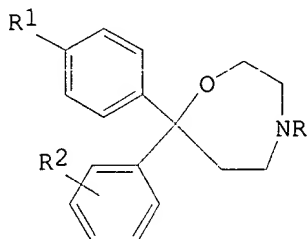
TITLE: Fluoxetine inhibits the metabolism of
tolterodine-pharmacokinetic implications and proposed
clinical relevance
AUTHOR(S): Brynne, N.; Svanstrom, C.; Aberg-Wistedt, A.; Hallen,
B.; Bertilsson, L.
CORPORATE SOURCE: Departments of Clinical Pharmacology, Pharmacia and
Upjohn AB, Stockholm, SE-112 87, Swed.
SOURCE: British Journal of Clinical Pharmacology (1999),
48(4), 553-563
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The change in disposition of tolterodine during coadministration of the
potent cytochrome P 450 2D6 (CYP2D6) inhibitor fluoxetine was studied.
Thirteen patients received tolterodine L-tartrate 2 mg twice daily for 2.5
days, followed by fluoxetine 20 mg once daily for 3 wk and then
concomitant administration for an addnl. 2.5 days. They were
characterized as extensive metabolizers (EM1 with one functional CYP2D6
gene, EM2 with two functional genes) or poor metabolizers (PM). Nine
patients, three EM2 and four EM1 and two PM, completed the trial.
Following tolterodine administration, the area under the serum concentration-time
curve (AUC) of tolterodine was 4.4-times and 30-times higher among EM1 and
PM, resp., compared with EM2. The AUC of the 5-hydroxymethyl metabolite
(5-HM) was not quantifiable in PM. Fluoxetine significantly decreased (P
 < 0.002) the oral clearance of tolterodine by 93% in EM2 and by 80% in
EM1. The AUC of 5-HM increased in EM2 and decreased in EM1. However, the
exposure to the active moiety (unbound tolterodine +5-HM) was not
significantly increased in the two phenotypes. The subdivision of the EM
group showed a 2.1-fold increase in active moiety in EM2 but the exposure
was still similar to EM1 compared with before the interaction. The study
suggests a difference in the pharmacokinetics of tolterodine and its
5-hydroxymethyl metabolite depending on the number of functional CYP2D6
genes. Fluoxetine significantly inhibited the hydroxylation of
tolterodine. Despite the effect on the pharmacokinetics of tolterodine in
extensive metabolizers, the clin. effect is expected to be within normal
variation.

IT Drug interactions
(adverse; fluoxetine inhibits the metabolism of tolterodine-
pharmacokinetics)
IT **Antidepressants**
Muscarinic antagonists
(fluoxetine inhibits the metabolism of tolterodine-pharmacokinetics)
IT Bladder
(incontinence; fluoxetine inhibits the metabolism of tolterodine-
pharmacokinetics)
IT Drug interactions
(pharmacokinetic; fluoxetine inhibits the metabolism of
tolterodine-pharmacokinetics)
IT 9035-51-2, Cytochrome P450, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(CYP2D6; fluoxetine inhibits the metabolism of tolterodine-
pharmacokinetics)
IT 54910-89-3, Fluoxetine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(fluoxetine inhibits the metabolism of tolterodine-pharmacokinetics)
IT 124937-51-5, Tolterodine 124937-52-6
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
BSU (Biological study, unclassified); BIOL (Biological study); PROC
(Process)
(fluoxetine inhibits the metabolism of tolterodine-pharmacokinetics)
IT **194482-41-2 194482-42-3 194482-43-4**
194482-44-5 207679-81-0, PNU-200577
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(fluoxetine inhibits the metabolism of tolterodine-pharmacokinetics)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1977:453414 CAPLUS
 DOCUMENT NUMBER: 87:53414
 TITLE: 1,4-Oxazepines
 INVENTOR(S): Bowman, Robert Mathews
 PATENT ASSIGNEE(S): Ciba-Geigy Corp., USA
 SOURCE: U.S., 10 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------------|------|----------|-----------------|-------------|
| US 4010166 | A | 19770301 | US 1975-615255 | 19750922 |
| US 3988448 | A | 19761026 | US 1974-526758 | 19741125 |
| ZA 7506191 | A | 19760929 | ZA 1975-6191 | 19750930 |
| DK 7505052 | A | 19760526 | DK 1975-5052 | 19751110 |
| FI 7503182 | A | 19760526 | FI 1975-3182 | 19751112 |
| SE 7512746 | A | 19760526 | SE 1975-12746 | 19751113 |
| NL 7513530 | A | 19760528 | NL 1975-13530 | 19751119 |
| NO 7503927 | A | 19760526 | NO 1975-3927 | 19751121 |
| BE 835855 | A1 | 19760524 | BE 1975-162108 | 19751124 |
| ZA 7507368 | A | 19761124 | ZA 1975-7368 | 19751124 |
| JP 51076283 | A2 | 19760701 | JP 1975-140361 | 19751125 |
| PRIORITY APPLN. INFO.: GI | | | US 1974-526758 | A2 19741125 |



I

AB The oxazepines I (R = PhCH₂, Me, allyl, Me₂C:CHCH₂, HC.tplbond.CCH₂, cyclopropylmethyl, PhCH₂CH₂, furfuryl, etc.; R₁ = H, F; R₂ = 2-MeO, 3-MeO, 3,4,5-(MeO)₃, 3-Cl, 4-F) were prepared. Thus, HOcPh₂CH₂CN was reduced and treated with PhCOCl followed by reduction and the HOcPh₂CH₂CH₂NHCH₂Ph treated with ClCH₂COCl to give HOcPh₂CH₂CH₂N(CH₂Ph)COCH₂Cl, which was cyclized and the 4-benzyl-3-oxo-7,7-diphenylhexahydro-1,4-oxazepine reduced with LiAlH₄ to give I (R = PhCH₂, R₁ = R₂ = H). At 20 mg/kg I were

antidepressants.

IT **Antidepressants**

(diphenylhexahydrooxazepines)

IT 60163-54-4 60163-68-0 60163-69-1 60163-70-4 60163-71-5
60280-67-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of)

IT 119-61-9, reactions 345-92-6 579-74-8 586-37-8 1136-86-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with acetonitrile)

IT 75-05-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with benzophenone)

IT 100-52-7, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with hydroxydiphenylpropylamine)

IT 60163-47-5P 60163-48-6P 60163-49-7P 60163-50-0P 60163-51-1P
60163-52-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and cyclization of, oxazepine derivative from)

IT 60163-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)

IT 63292-46-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)

IT 60163-56-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of, oxazepine derivative from)

IT 60163-22-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)

IT 4320-44-9P 50775-34-3P 60163-33-9P 60163-34-0P 60163-35-1P
60163-36-2P 60163-60-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with benzoyl chloride)

IT 60163-40-8P 60163-41-9P 60163-42-0P 60163-43-1P 60163-44-2P
60163-61-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with chloroacetyl chloride)

IT 63292-52-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with diethylamine)

IT 60163-57-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with ethyl chloroformate)

IT 3531-23-5P 50775-33-2P 60163-21-5P 60163-29-3P 60163-30-6P
60163-31-7P 60163-32-8P 60163-37-3P **60163-38-4P**
60163-39-5P 60163-53-3P 60163-59-9P 60163-62-4P 60163-63-5P
60181-44-4P 62537-40-0P 63292-45-5P 63292-47-7P 63292-48-8P
63292-49-9P 63292-50-2P 63292-60-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

IT 60162-87-0P 60162-88-1P 60162-89-2P 60162-90-5P 60162-91-6P
60162-92-7P 60162-93-8P 60162-94-9P 60162-95-0P 60162-96-1P
60162-97-2P 60162-98-3P 60162-99-4P 60163-00-0P 60163-01-1P
60163-02-2P 60163-03-3P 60163-04-4P 60163-05-5P 60163-06-6P
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60163-15-7P 60163-16-8P 60163-17-9P 60163-18-0P 60163-19-1P
60163-20-4P 60163-23-7P 60163-24-8P 60163-26-0P 60163-27-1P
60163-28-2P 60163-46-4P 60163-65-7P 62537-12-6P 63292-51-3P
63292-54-6P 63292-55-7P 63292-56-8P 63292-58-0P 63292-59-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 60163-65-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with allyl bromide)

IT 541-41-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzyldiphenylhexahydrooxazepine)

IT 79-04-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzylhydroxydiphenylpropylamines)

IT 124-40-3, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chloroacetyldiphenylhexahydrooxazepine)

IT 75-21-8, reactions 107-13-1, reactions 107-14-2 2094-72-6
3874-54-2

RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with dipenylhexahydrooxazepine)
 IT 106-95-6, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with diphenylhexahydrooxazepine)
 IT 75-21-8, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with hexahydrodiphenyloxazepine)
 IT 51806-20-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with hydroxydiphenylpropionitrile)
 IT 98-88-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with hydroxydiphenylpropylamines)

L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:388157 CAPLUS

DOCUMENT NUMBER: 131:44658

TITLE: Preparation of bis(fluorophenyl)alkylamides as
 anticonvulsants and central nervous system agents.

INVENTOR(S): Balandrin, Manuel F.; Vanwagenen, Bradford C.; Artman,
 Linda D.; Mueller, Alan L.; Smith, Daryl

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

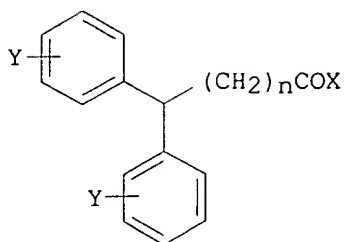
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9929657 | A1 | 19990617 | WO 1998-US26315 | 19981209 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2313236 | AA | 19990617 | CA 1998-2313236 | 19981209 |
| AU 9918170 | A1 | 19990628 | AU 1999-18170 | 19981209 |
| AU 763245 | B2 | 20030717 | | |
| EP 1042275 | A1 | 20001011 | EP 1998-963065 | 19981209 |
| EP 1042275 | B1 | 20051109 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001525390 | T2 | 20011211 | JP 2000-524254 | 19981209 |
| NZ 524395 | A | 20041029 | NZ 1998-524395 | 19981209 |
| IL 136306 | A1 | 20050925 | IL 1998-136306 | 19981209 |
| AT 309200 | E | 20051115 | AT 1998-963065 | 19981209 |
| US 6617358 | B1 | 20030909 | US 2000-587179 | 20000602 |
| US 2003199589 | A1 | 20031023 | US 2003-429060 | 20030502 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1997-69005P | P 19971210 |
| | | | WO 1998-US26315 | W 19981209 |
| | | | US 2000-587179 | A1 20000602 |

OTHER SOURCE(S): MARPAT 131:44658

GI



AB Title compds. (I; Y = H, F, Cl; X = NR₁R₂, OR₁; R₁ = H, alkyl, hydroxyalkyl; R₂ = H, Me, Et; n = 0-4; with specific exceptions), were prepared for treatment of seizure disorder, neurodegenerative disease, anxiety, stress, multiple sclerosis, Parkinson's disease, migraine, etc. (no data). Thus, 4,4-bis(4-fluorophenyl)butyl chloride was treated successively with KOAc in DMF, NaOH in EtOH/H₂O, CrO₃/H₂SO₄ in H₂O/acetone, SOCl₂, and NH₃ in H₂O/EtOAc to give 4,4-bis(4-fluorophenyl)butanamide.

IT Nervous system
(Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system
(amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Spinal cord
(injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
(~~manic~~ bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
(~~mood~~-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Anti-Alzheimer's agents
Anticonvulsants
Antimigraine agents
Antiparkinsonian agents
Anxiolytics
Nervous system agents
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Brain, disease
(stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Head
(trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Multiple sclerosis
(treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P
200429-53-4P 200429-54-5P 200429-55-6P 227289-95-4P
227290-02-0P 227290-09-7P 227290-12-2P
 227290-22-4P 227290-28-0P 227290-37-1P 227290-41-7P 227290-47-3P
 227290-50-8P 227290-56-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions
 124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,
 4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,
 Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,

Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate
3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central
nervous system agents)

IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P
50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P
170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-
fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P
227290-64-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central
nervous system agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2000:9954 USPATFULL

TITLE: Compounds active at a novel site on receptor-operated
calcium channels useful for treatment of neurological
disorders and diseases

INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, United States
Balandrin, Manuel F., Sandy, UT, United States
VanWagenen, Bradford C., Salt Lake City, UT, United
States
Moe, Scott T., Salt Lake City, UT, United States
DelMar, Eric G., Salt Lake City, UT, United States
Artman, Linda D., Salt Lake City, UT, United States
Barmore, Robert M., Salt Lake City, UT, United States
Smith, Daryl L., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United
States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6017965 | | 20000125 |
| APPLICATION INFO.: | US 1996-763480 | | 19961211 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1996-663013, filed on 7 Jun 1996 which is a continuation-in-part of Ser. No. US 1995-485038, filed on 7 Jun 1995 which is a continuation-in-part of Ser. No. WO 1994-US12293, filed on 26 Oct 1994 which is a continuation-in-part of Ser. No. US 1994-288668, filed on 9 Aug 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-194210, filed on 8 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-14813, filed on 8 Feb 1993, now abandoned | | |

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: Lyon & Lyon LLP
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
LINE COUNT: 6207

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method and compositions for treating a patient having a neurological
disease or disorder, such as stroke, head trauma, spinal cord injury,
spinal cord ischemia, ischemia- or hypoxia-induced nerve cell damage,
epilepsy, anxiety, neuropsychiatric or cognitive deficits due to
ischemia or hypoxia such as those that frequently occur as a consequence
of cardiac surgery under cardiopulmonary bypass, or neurodegenerative
diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's
Disease, or amyotrophic lateral sclerosis (ALS).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Calcium channel
(NMDA-binding glutamate receptor complex, antagonists; preparation of
aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
(NMDA-binding, calcium channel complexes, antagonists; preparation of
aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Nervous system
(disease, treatment; preparation of aralkylamines as NMDA receptor-ionophore
complex antagonists)

IT Glutamate receptors
(methyl-D-aspartate-binding, calcium channel complexes, antagonists;
preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Cytoprotective agents
(neuroprotectants; preparation of aralkylamines as NMDA receptor-ionophore
complex antagonists)

IT Analgesics

IT Anticonvulsants
(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

IT 5586-73-2P, 3,3-Diphenylpropylamine
(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
5666-18-2P 14451-09-3P, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
17349-94-9P 19841-73-7P 21745-77-7P, 9H-Xanthene-9-ethanamine
21745-81-3P, 9H-Thioxanthene-9-ethanamine 21745-82-4P 21745-83-5P
21745-85-7P 28075-29-8P 36765-74-9P 48166-95-6P 53179-07-0P
54910-89-3P 57226-64-9P 63940-51-2P 64630-52-0P 90531-05-8P
91472-94-5P 95956-62-0P 98383-47-2P 98383-56-3P 106359-50-6P
109306-10-7P 114754-01-7P 114754-02-8P 114754-03-9P 114754-04-0P
118468-16-9P 144451-90-1P 144451-98-9P 144452-04-0P 144452-11-9P
159149-65-2P 170018-54-9P 170018-55-0P **170018-56-1P**
170018-57-2P 170018-63-0P 170018-66-3P 170018-67-4P 170018-68-5P
170018-71-0P **170018-72-1P** **170018-73-2P** 170018-74-3P
170018-75-4P 170018-76-5P 170018-77-6P 170018-78-7P
170018-79-8P 170018-80-1P 170018-81-2P 170018-82-3P 170018-83-4P
170018-84-5P 170018-85-6P 170018-86-7P 170019-10-0P 186495-37-4P
186495-38-5P 186495-39-6P 186495-40-9P 186495-41-0P 186495-42-1P
186495-43-2P **186495-44-3P** 186495-45-4P 186495-46-5P
186495-47-6P **186495-48-7P** 186495-49-8P 186495-50-1P
186495-51-2P 186495-52-3P 186495-53-4P 186495-54-5P 186495-55-6P
186495-56-7P 186495-57-8P **186495-58-9P** 186495-59-0P
186495-60-3P 186495-61-4P 186495-62-5P 186495-63-6P
186495-64-7P 186495-65-8P 186495-66-9P 186495-67-0P 186495-68-1P
186495-69-2P 186495-70-5P 186495-71-6P 186495-72-7P 186495-73-8P
186495-74-9P 186495-75-0P 186495-76-1P 186495-77-2P
186495-78-3P 186495-79-4P 186495-80-7P **186495-81-8P**
186495-82-9P 186495-84-1P 186495-86-3P 186495-87-4P 186495-88-5P
186495-89-6P 186495-90-9P 186495-91-0P 186495-92-1P 186495-93-2P
186495-94-3P 186495-95-4P 186495-97-6P **186495-98-7P**
186495-99-8P 186496-00-4P 186496-01-5P 186496-02-6P 186496-03-7P
186496-04-8P 186496-05-9P 186496-06-0P **186496-07-1P**
186496-08-2P 186496-09-3P 186496-10-6P 186496-11-7P
186496-12-8P 186496-13-9P 186496-14-0P 186496-15-1P 186496-16-2P
186496-17-3P 186496-20-8P 186496-21-9P 186496-22-0P 186496-23-1P
186496-24-2P 186496-25-3P 186496-26-4P 186496-27-5P 186496-29-7P
186496-30-0P 186496-71-9P **200420-69-5P** 200427-53-8P
200429-46-5P 200429-48-7P 200429-49-8P 200429-50-1P 200429-51-2P
200429-52-3P **200429-53-4P** 200429-54-5P 200429-55-6P
200429-56-7P 200429-57-8P 200429-58-9P 200429-59-0P 200429-60-3P
200429-61-4P 200429-62-5P 200429-63-6P 200429-64-7P 200429-65-8P
200429-67-0P 200429-68-1P 200429-69-2P 200429-70-5P 200429-71-6P
200429-72-7P 200429-73-8P 200429-74-9P 200429-75-0P 200429-79-4P
200429-80-7P 200429-86-3P 200429-87-4P 200430-04-2P 200430-05-3P
200430-06-4P 200430-07-5P 200430-08-6P 200430-14-4P 200430-16-6P
200430-18-8P 200430-19-9P
(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

IT 85-41-6, Phthalimide 103-67-3, N-Methylbenzylamine 135-02-4,
o-Anisaldehyde 140-88-5 285-67-6, Cyclopentene oxide 345-70-0,
3,3'-Difluorobenzophenone 351-54-2, 3-Fluoro-p-anisaldehyde 372-20-3,
3-Fluorophenol 452-08-4, 2-Bromo-4-fluoroanisole 456-48-4,

3-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 578-57-4,
 2-Bromoanisole 587-04-2, 3-Chlorobenzaldehyde 610-99-1 932-31-0,
 2-Methylphenylmagnesium bromide 1073-06-9, 1-Bromo-3-fluorobenzene
 1210-35-1, Dibenzosuberone 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one
 17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2,
 (S)-N-Benzyl- α -methylbenzylamine 18707-60-3, Methyl crotonate
 20595-30-6, Trans-3-Fluorocinnamic acid 21900-39-0,
 5-Fluoro-2-methylbenzoyl chloride 65416-24-2, Benzyl crotonate
 77532-79-7, 5-Fluoro-2-methylbenzonitrile 100306-34-1 147624-13-3,
 3-Fluoro-2-methylbenzaldehyde 170019-09-7, 3,3-Bis(3-
 fluorophenyl)propionitrile 186496-59-3, 5-Fluoro-2-
 methylphenylmagnesium bromide

(preparation of aralkylamines as NMDA receptor-ionophore complex
 antagonists)

IT 455-67-4P 458-45-7P 701-38-2P 5561-92-2P, 1-(2-Methoxyphenyl)-1-
 propanone 15966-37-7P 21745-42-6P 21745-68-6P 25772-94-5P
 38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P
 156868-83-6P, 3-(3-Fluorophenyl)-1-propanol 170019-11-1P
 170019-14-4P, Ethyl 3,3-bis(3-fluorophenyl)propionate 170019-15-5P
 170019-16-6P 170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P
 170019-21-3P 170019-22-4P 170019-23-5P 170019-24-6P 170019-25-7P
 186496-34-4P 186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P
 186496-39-9P 186496-40-2P 186496-41-3P 186496-42-4P 186496-44-6P
 186496-45-7P 186496-46-8P **186496-48-0P** 186496-49-1P
 186496-50-4P 186496-51-5P 186496-52-6P 186496-53-7P 186496-57-1P
 186496-58-2P 186496-60-6P 200430-09-7P 200430-10-0P 200430-11-1P
 200430-12-2P, 3,3'-Difluoro-4-methoxybenzophenone 200430-13-3P
200430-15-5P 200430-17-7P

(preparation of aralkylamines as NMDA receptor-ionophore complex
 antagonists)

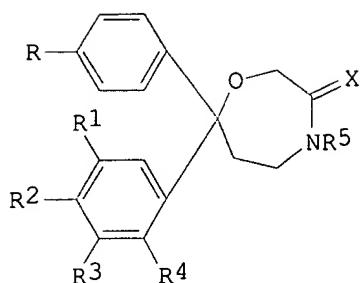
L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1977:171519 CAPLUS
 DOCUMENT NUMBER: 86:171519
 TITLE: 7,7-Diphenyl hexahydro-1,4-oxazepines
 INVENTOR(S): Bowman, Robert M.
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
 SOURCE: Fr. Demande, 30 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| FR 2291759 | A1 | 19760618 | FR 1975-35647 | 19751121 |
| US 3988448 | A | 19761026 | US 1974-526758 | 19741125 |
| ZA 7506191 | A | 19760929 | ZA 1975-6191 | 19750930 |
| DK 7505052 | A | 19760526 | DK 1975-5052 | 19751110 |
| FI 7503182 | A | 19760526 | FI 1975-3182 | 19751112 |
| SE 7512746 | A | 19760526 | SE 1975-12746 | 19751113 |
| NL 7513530 | A | 19760528 | NL 1975-13530 | 19751119 |
| NO 7503927 | A | 19760526 | NO 1975-3927 | 19751121 |
| BE 835855 | A1 | 19760524 | BE 1975-162108 | 19751124 |
| ZA 7507368 | A | 19761124 | ZA 1975-7368 | 19751124 |
| JP 51076283 | A2 | 19760701 | JP 1975-140361 | 19751125 |

PRIORITY APPLN. INFO.: US 1974-526758 A 19741125

GI



I

AB Oxazepines I (R = H, F; R1 = H, MeO, Cl, F; R2,R4 = H, MeO; R3 = H, F, MeO; R5 = PhCH2, Me, allyl, Me2C:CHCH2, propargyl, PhCH2CH, MeCH:CHCH2, PhCH:CHCH2, EtCOCH2, ClCH:CHCH2, furfuryl; X = H2) (26 compds.), useful as **antidepressants**, were prepared by reduction of I (X = O). Thus, LiAlH4 reduction of I (R-R4 = H, R5 = PhCH2, X = O) gave I (R-R4 = H, R5 = PhCH2 X = H2), isolated as HCl salt.

IT **Antidepressants**

(diphenylhexahydro-1,4-oxazepines)

IT 4023-34-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of (aminopropoxy)acetaldehyde acetal)

IT 79-04-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by, of benzyl hydroxydiphenylpropylamines)

IT 106-95-6, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of (hydroxyphenyl)phenylhexahydrooxazepine)

IT 106-95-6, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of diphenylhexahydrooxazepine)

IT 60163-54-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, by allyl bromide)

IT 60163-65-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(allylation of)

IT 119-61-9, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with acetonitrile)

IT 75-05-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with benzophenone)

IT 60163-24-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with chloroacetonitrile)

IT 75-21-8, reactions 107-13-1, reactions 107-14-2 3874-54-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with diphenylhexahydrooxazepine)

IT 51806-20-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with hydroxydiphenylpropionitrile)

IT 3531-23-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with iodoacetaldehyde diethyl acetal)

IT 4320-44-9

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with benzaldehyde)

IT 100-52-7, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with hydroxydiphenylpropylamine)

IT 60163-61-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

IT 60163-40-8P 60163-41-9P 60163-42-0P 60163-43-1P 60163-44-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
 (preparation and acylation of, by chloroacetyl chloride)

IT 60163-56-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and acylation of, by cyclopropanecarbonyl chloride)

IT 4320-44-9P 50775-34-3P 60163-33-9P 60163-34-0P 60163-36-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and benzoylation of)

IT 60163-60-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and benzylation of)

IT 60163-54-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and condensation of, with halo butyrophenone)

IT 60163-47-5P 60163-48-6P 60163-49-7P 60163-50-0P 60163-51-1P
 60163-52-2P 60163-62-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and cyclization of)

IT 60163-58-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and ethylation of)

IT 3531-23-5P 50775-33-2P 60163-21-5P 60163-29-3P 60163-30-6P
 60163-32-8P 60163-37-3P **60163-38-4P** 60163-39-5P
 60163-53-3P 60163-55-5P 60163-66-8P 60181-44-4P 63292-45-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and hydride reduction of)

IT 62537-30-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and hydrogenation of)

IT 60163-64-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and hydrogenolysis of)

IT 60163-59-9P 60163-63-5P 62537-40-0P 63292-47-7P 63292-48-8P
 63292-49-9P 63292-50-2P 63292-60-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reduction of)

IT 60163-56-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reductive cyclization of)

IT 60162-87-0P 60162-88-1P 60162-89-2P 60162-90-5P 60162-91-6P
 60162-92-7P 60162-93-8P 60162-95-0P 60162-96-1P 60162-97-2P
 60162-98-3P 60162-99-4P 60163-00-0P 60163-01-1P 60163-02-2P
 60163-03-3P 60163-04-4P 60163-06-6P 60163-08-8P 60163-12-4P
 60163-13-5P 60163-14-6P 60163-15-7P 60163-16-8P 60163-17-9P
 60163-18-0P 60163-19-1P 60163-20-4P 60163-25-9P 60163-26-0P
 60163-27-1P 60163-28-2P 60163-31-7P 60163-46-4P 60163-57-7P
 60163-65-7P 60163-67-9P 62537-09-1P 62537-10-4P 62537-11-5P
 62537-12-6P 62537-41-1P 62537-42-2P 62537-43-3P 62537-44-4P
 63292-51-3P 63292-59-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

IT 62537-54-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reductive cyclization of)

L8 ANSWER 7 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2003:283245 USPATFULL

TITLE: Anticonvulsant and central nervous system-depressing
 bis (fluorophenyl) alkylamides and their uses

INVENTOR(S): Balandrin, Manuel F., Sandy, UT, UNITED STATES
 VanWagenen, Bradford C., Salt Lake City, UT, UNITED STATES
 Artman, Linda D., Salt Lake City, UT, UNITED STATES
 Mueller, Alan L., Salt Lake City, UT, UNITED STATES
 Smith, Daryl, Salt Lake City, UT, UNITED STATES
 Moe, Scott T., Boston, MA, UNITED STATES
 PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc. (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2003199589 | A1 | 20031023 |
| APPLICATION INFO.: | US 2003-429060 | A1 | 20030502 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2000-587179, filed on 2 Jun 2000, PENDING Continuation of Ser. No. WO 1998-US26315, filed on 9 Dec 1998, PENDING | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1997-69005P | 19971210 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | NPS PHARMACEUTICALS, INC. C/O FOLEY & LARDNER, P.O. BOX 80278, SAN DIEGO, CA, 92138-0278 | |
| NUMBER OF CLAIMS: | 30 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 4 Drawing Page(s) | |
| LINE COUNT: | 1342 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Bis(Fluorophenyl)alkylamides have been chemically synthesized which possess beneficial pharmacological properties (e.g., anticonvulsant activity) useful for the treatment of neurological diseases or disorders, such as, for example, epilepsy, convulsions, and seizure disorders. The preferred compounds of the invention also cause little sedation and have high therapeutic and protective indices in animal models of epilepsy. These compounds further possess long pharmacologic half-lives, which, in practical clinical therapeutic application, should translate into once-a-day dosing, of great benefit to patients suffering from these diseases and/or disorders. These compounds may also be of further clinical utility in the treatment of other diseases and disorders of the central and peripheral nervous systems, or diseases or disorders affected by them, including, but not limited to, spasticity, skeletal muscle spasms and pain, restless leg syndrome, anxiety and stress, and bipolar disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Nervous system
 (Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system
 (amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Spinal cord
 (injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (manic bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (mood-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Anti-Alzheimer's agents

IT Anticonvulsants

IT Antimigraine agents

IT Antiparkinsonian agents

IT Anxiolytics

IT Nervous system agents

(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Brain, disease

(stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Head

(trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Multiple sclerosis

(treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P

200429-53-4P 200429-54-5P 200429-55-6P 227289-95-4P

227290-02-0P 227290-09-7P 227290-12-2P

227290-22-4P 227290-28-0P 227290-37-1P 227290-41-7P 227290-47-3P

227290-50-8P 227290-56-4P

(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions

124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,

4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,

Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,

Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate

3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride

(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P

50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P

170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-

fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P

227290-64-4P

(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

L8 ANSWER 8 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2003:240418 USPATFULL

TITLE: Anticonvulsant and central nervous system-depressing bis(fluorophenyl)alkylamides and their uses

INVENTOR(S): Balandrin, Manuel F., Sandy, UT, United States
VanWagenen, Bradford C., Salt Lake City, UT, United States

Artman, Linda D., Salt Lake City, UT, United States

Mueller, Alan L., Salt Lake City, UT, United States

Smith, Daryl, Salt Lake City, UT, United States

Moe, Scott T., Salt Lake City, UT, United States

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6617358 | B1 | 20030909 |
| APPLICATION INFO.: | US 2000-587179 | | 20000602 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. WO 1998-US26315, filed on 9 Dec 1998 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1997-69005P | 19971210 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Kumar, Shailendra | |
| NUMBER OF CLAIMS: | 19 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 9 Drawing Figure(s); 8 Drawing Page(s) | |
| LINE COUNT: | 1387 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Bis(Fluorophenyl)alkylamides have been chemically synthesized which possess beneficial pharmacological properties (e.g., anticonvulsant activity) useful for the treatment of neurological diseases or

disorders, such as, for example, epilepsy, convulsions, and seizure disorders. The preferred compounds of the invention also cause little sedation and have high therapeutic and protective indices in animal models of epilepsy. These compounds further possess long pharmacological half-lives, which, in practical clinical therapeutic application, should translate into once-a-day dosing, of great benefit to patients suffering from these diseases and/or disorders. These compounds may also be of further clinical utility in the treatment of other diseases and disorders of the central and peripheral nervous systems, or diseases or disorders affected by them, including, but not limited to, spasticity, skeletal muscle spasms and pain, restless leg syndrome, anxiety and stress, and bipolar disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Nervous system
(Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system
(amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Spinal cord
(injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
(manic bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
(mood-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Anti-Alzheimer's agents

IT Anticonvulsants

IT Antimigraine agents

IT Antiparkinsonian agents

IT Anxiolytics

IT Nervous system agents
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Brain, disease
(stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Head
(trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Multiple sclerosis
(treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P
200429-53-4P 200429-54-5P 200429-55-6P **227289-95-4P**
227290-02-0P 227290-09-7P 227290-12-2P
 227290-22-4P 227290-28-0P 227290-37-1P 227290-41-7P 227290-47-3P
 227290-50-8P 227290-56-4P
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions
 124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,
 4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,
 Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,
 Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate
 3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P
 50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P
 170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P
 227290-64-4P
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central

nervous system agents)

L8 ANSWER 9 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2004:221898 USPATFULL

TITLE: Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, UNITED STATES

Moe, Scott T., Salt Lake City, UT, UNITED STATES

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc. (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|---------------|
| PATENT INFORMATION: | US 2004171670 | A1 | 20040902 |
| APPLICATION INFO.: | US 2004-797355 | A1 | 20040309 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2001-825373, filed on 2 Apr 2001, GRANTED, Pat. No. US 6750244 Continuation of Ser. No. US 1998-186341, filed on 4 Nov 1998, GRANTED, Pat. No. US 6211245 Continuation of Ser. No. US 1997-873011, filed on 11 Jun 1997, ABANDONED Continuation-in-part of Ser. No. US 1997-869154, filed on 4 Jun 1997, ABANDONED Continuation-in-part of Ser. No. US 1996-763480, filed on 11 Dec 1996, GRANTED, Pat. No. US 6017965 Continuation-in-part of Ser. No. US 1996-663013, filed on 7 Jun 1996, ABANDONED Continuation-in-part of Ser. No. US 1995-485038, filed on 7 Jun 1995, GRANTED, Pat. No. US 6071970 | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | NPS PHARMACEUTICALS, INC. C/O FOLEY & LARDNER, P.O. BOX 80278, SAN DIEGO, CA, 92138-0278 | | |
| NUMBER OF CLAIMS: | 1 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 6301 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method and compositions for treating a patient having a neurological disease or disorder, such as stroke, head trauma, spinal cord injury, spinal cord ischemia, ischemia- or hypoxia-induced nerve cell damage, epilepsy, anxiety, neuropsychiatric or cognitive deficits due to ischemia or hypoxia such as those that frequently occur as a consequence of cardiac surgery under cardiopulmonary bypass, or neurodegenerative diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's Disease, or amyotrophic lateral sclerosis (ALS).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Analgesics

IT Anticonvulsants and Antiepileptics

IT Anxiolytics

IT Muscle relaxants

IT Nervous system agents

(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Receptors

(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Amines, biological studies

(aralkyl, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Ion channel

(calcium, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Anesthetics

(general, adjuncts; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Receptors
(glutamatergic, AMPA-binding, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Receptors
(glutamatergic, kainate-binding, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Receptors
(glutamatergic, methyl-D-aspartate-binding, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Cytoprotective agents
(neuroprotectants, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT Receptors
(nicotinic, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-39-0P 170018-44-7P 170018-47-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 133805-32-0 144576-90-9 148920-48-3 170018-49-2
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 144451-98-9P 170018-46-9P 170018-54-9P 170018-55-0P 170018-57-2P
170018-63-0P 170018-68-5P 170018-71-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 5586-73-2 170018-40-3 170018-41-4 170018-42-5 170018-43-6
170018-45-8 170018-50-5 170018-51-6 170018-52-7 170018-53-8
170018-56-1 170018-58-3 170018-59-4 170018-60-7
170018-61-8 170018-62-9 170018-64-1 170018-70-9 170018-74-3
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 7440-70-2, Calcium, biological studies
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 14209-32-6P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 100-02-7, p-Nitrophenol, reactions 100-52-7, Benzaldehyde, reactions
107-13-1, 2-Propenenitrile, reactions 109-76-2, 1,3-Propanediamine
110-60-1, 1,4-Diaminobutane 135-02-4, o-Anisaldehyde 345-70-0,
3,3'-Difluorobenzophenone 456-48-4, 3-Fluorobenzaldehyde 462-94-2,
1,5-Pentanediamine 557-66-4, Ethylamine hydrochloride 587-04-2,
3-Chlorobenzaldehyde 1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1
5003-71-4 5460-29-7, N-(3-Bromopropyl)phthalimide 7300-34-7,
4,9-Dioxa-1,12-dodecanediamine 24424-99-5, Di-tert-butyl dicarbonate
99532-53-3 170019-09-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 455-67-4P 701-38-2P 4748-73-6P 38158-77-9P 51644-96-3P
75762-57-1P 83948-53-2P 101187-29-5P 105628-63-5P 114459-62-0P
122248-82-2P 122631-98-5P 122632-01-3P 122632-02-4P 128550-02-7P
128550-03-8P 128550-05-0P 128550-06-1P 144923-52-4P 147875-12-5P
147875-14-7P 147875-27-2P 170018-87-8P 170018-88-9P 170018-89-0P
170018-90-3P 170018-91-4P 170018-92-5P 170018-93-6P 170018-96-9P
170018-97-0P 170018-98-1P 170018-99-2P 170019-00-8P 170019-01-9P
170019-02-0P 170019-03-1P 170019-04-2P 170019-05-3P 170019-06-4P

170019-07-5P 170019-08-6P 170019-11-1P 170019-12-2P 170019-13-3P
170019-14-4P 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P
170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P
170019-24-6P 170019-25-7P

(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-95-8P 170019-10-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-66-3P 170018-67-4P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-48-1 170018-65-2 170018-69-6 **170018-72-1**
170018-73-2 170018-75-4 170018-76-5 170018-77-6
170018-78-7 170018-79-8 170018-80-1 170018-81-2 170018-82-3
170018-83-4 170018-84-5 170018-85-6 170018-86-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

L8 ANSWER 10 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2002:8522 USPATFULL

TITLE: Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, UNITED STATES

Moe, Scott T., Salt Lake City, UT, UNITED STATES

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc. (U.S. corporation)

| | NUMBER | KIND | DATE |
|--|---|------|--------------|
| PATENT INFORMATION: | US 2002004522 | A1 | 20020110 |
| | US 6750244 | B2 | 20040615 |
| APPLICATION INFO.: | US 2001-825373 | A1 | 20010402 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1998-186341, filed on 4 Nov 1998, GRANTED, Pat. No. US 6211245 Continuation of Ser. No. US 1997-873011, filed on 11 Jun 1997, ABANDONED Continuation-in-part of Ser. No. US 1996-763480, filed on 11 Dec 1996, GRANTED, Pat. No. US 6017965 Continuation-in-part of Ser. No. US 1996-663013, filed on 7 Jun 1996, ABANDONED Continuation-in-part of Ser. No. US 1995-485038, filed on 7 Jun 1995, GRANTED, Pat. No. US 6071970 Continuation-in-part of Ser. No. WO 1994-US12293, filed on 26 Oct 1994, UNKNOWN Continuation-in-part of Ser. No. US 1994-288688, filed on 11 Aug 1994, GRANTED, Pat. No. US 5544872 Continuation-in-part of Ser. No. US 1994-194210, filed on 8 Feb 1994, ABANDONED Continuation-in-part of Ser. No. US 1993-14813, filed on 8 Feb 1993, ABANDONED | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | Foley & Lardner, 23rd Floor, 402 W. Broadway, San Diego, CA, 92101-3542 | | |
| NUMBER OF CLAIMS: | 31 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 6312 | | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | | |

AB Method and compositions for treating a patient having a neurological disease or disorder, such as stroke, head trauma, spinal cord injury, spinal cord ischemia, ischemia- or hypoxia-induced nerve cell damage, epilepsy, anxiety, neuropsychiatric or cognitive deficits due to ischemia or hypoxia such as those that frequently occur as a consequence of cardiac surgery under cardiopulmonary bypass, or neurodegenerative diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's Disease, or amyotrophic lateral sclerosis (ALS).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Analgesics
IT Anticonvulsants and Antiepileptics
IT Anxiolytics
IT Muscle relaxants
IT Nervous system agents
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Amines, biological studies
 (aralkyl, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Ion channel
 (calcium, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Anesthetics
 (general, adjuncts; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
 (glutamatergic, AMPA-binding, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
 (glutamatergic, kainate-binding, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
 (glutamatergic, methyl-D-aspartate-binding, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Cytoprotective agents
 (neuroprotectants, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
 (nicotinic, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 170018-39-0P 170018-44-7P 170018-47-0P
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 133805-32-0 144576-90-9 148920-48-3 170018-49-2
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 144451-98-9P 170018-46-9P 170018-54-9P 170018-55-0P 170018-57-2P
170018-63-0P 170018-68-5P 170018-71-0P
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 5586-73-2 170018-40-3 170018-41-4 170018-42-5 170018-43-6
170018-45-8 170018-50-5 170018-51-6 170018-52-7 170018-53-8
170018-56-1 170018-58-3 170018-59-4 170018-60-7
170018-61-8 170018-62-9 170018-64-1 170018-70-9 170018-74-3
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 7440-70-2, Calcium, biological studies
 (aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these

compsd.)

IT 14209-32-6P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 100-02-7, p-Nitrophenol, reactions 100-52-7, Benzaldehyde, reactions 107-13-1, 2-Propenenitrile, reactions 109-76-2, 1,3-Propanediamine 110-60-1, 1,4-Diaminobutane 135-02-4, o-Anisaldehyde 345-70-0, 3,3'-Difluorobenzophenone 456-48-4, 3-Fluorobenzaldehyde 462-94-2, 1,5-Pentanediamine 557-66-4, Ethylamine hydrochloride 587-04-2, 3-Chlorobenzaldehyde 1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1 5003-71-4 5460-29-7, N-(3-Bromopropyl)phthalimide 7300-34-7, 4,9-Dioxa-1,12-dodecanediamine 24424-99-5, Di-tert-butyl dicarbonate 99532-53-3 170019-09-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 455-67-4P 701-38-2P 4748-73-6P 38158-77-9P 51644-96-3P
75762-57-1P 83948-53-2P 101187-29-5P 105628-63-5P 114459-62-0P
122248-82-2P 122631-98-5P 122632-01-3P 122632-02-4P 128550-02-7P
128550-03-8P 128550-05-0P 128550-06-1P 144923-52-4P 147875-12-5P
147875-14-7P 147875-27-2P 170018-87-8P 170018-88-9P 170018-89-0P
170018-90-3P 170018-91-4P 170018-92-5P 170018-93-6P 170018-96-9P
170018-97-0P 170018-98-1P 170018-99-2P 170019-00-8P 170019-01-9P
170019-02-0P 170019-03-1P 170019-04-2P 170019-05-3P 170019-06-4P
170019-07-5P 170019-08-6P 170019-11-1P 170019-12-2P 170019-13-3P
170019-14-4P 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P
170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P
170019-24-6P 170019-25-7P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-95-8P 170019-10-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-66-3P 170018-67-4P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-48-1 170018-65-2 170018-69-6 **170018-72-1**
170018-73-2 170018-75-4 170018-76-5 170018-77-6
170018-78-7 170018-79-8 170018-80-1 170018-81-2 170018-82-3
170018-83-4 170018-84-5 170018-85-6 170018-86-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

L8 ANSWER 11 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2001:48118 USPATFULL

TITLE: Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, United States
Moe, Scott T., Salt Lake City, UT, United States

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6211245 | B1 | 20010403 |
| APPLICATION INFO.: | US 1998-186341 | | 19981104 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1997-873011, filed on 11 Jun 1997 | | |
| | Continuation-in-part of Ser. No. US 1997-869154, filed on 4 Jun 1997, now abandoned | | |
| | Continuation-in-part of Ser. No. US 1996-763480, filed on 11 Dec 1996, now patented, Pat. No. US 6017965 | | |
| | Continuation-in-part of Ser. No. US 1996-663013, filed on 7 Jun 1996, now abandoned | | |
| | Continuation-in-part of | | |

Ser. No. US 1995-485038, filed on 7 Jun 1995
Continuation-in-part of Ser. No. WO 1994-US12293, filed
on 26 Oct 1994 Continuation-in-part of Ser. No. US
1994-288668, filed on 9 Aug 1994, now abandoned
Continuation-in-part of Ser. No. US 1994-194210, filed
on 8 Feb 1994, now abandoned Continuation-in-part of
Ser. No. US 1993-14813, filed on 8 Feb 1993, now
abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
NUMBER OF CLAIMS: 45
EXEMPLARY CLAIM: 1
LINE COUNT: 6559

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method and compositions for treating a patient having a neurological
disease or disorder, such as stroke, head trauma, spinal cord injury,
spinal cord ischemia, ischemia- or hypoxia-induced nerve cell damage,
epilepsy, anxiety, neuropsychiatric or cognitive deficits due to
ischemia or hypoxia such as those that frequently occur as a consequence
of cardiac surgery under cardiopulmonary bypass, or neurodegenerative
diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's
Disease, or amyotrophic lateral sclerosis (ALS).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Analgesics
IT Anticonvulsants and Antiepileptics
IT Anxiolytics
IT Muscle relaxants
IT Nervous system agents
(aralkylamine compds. active at site on receptor-operated calcium
channels for treatment of neurol. disorders, and preparation of these
compds.)
IT Receptors
(aralkylamine compds. active at site on receptor-operated calcium
channels for treatment of neurol. disorders, and preparation of these
compds.)
IT Amines, biological studies
(aralkyl, aralkylamine compds. active at site on receptor-operated
calcium channels for treatment of neurol. disorders, and preparation of
these compds.)
IT Ion channel
(calcium, aralkylamine compds. active at site on receptor-operated
calcium channels for treatment of neurol. disorders, and preparation of
these compds.)
IT Anesthetics
(general, adjuncts; aralkylamine compds. active at site on
receptor-operated calcium channels for treatment of neurol. disorders,
and preparation of these compds.)
IT Receptors
(glutamatergic, AMPA-binding, ionophore complexes; aralkylamine compds.
active at site on receptor-operated calcium channels for treatment of
neurol. disorders, and preparation of these compds.)
IT Receptors
(glutamatergic, kainate-binding, aralkylamine compds. active at site on
receptor-operated calcium channels for treatment of neurol. disorders,
and preparation of these compds.)
IT Receptors
(glutamatergic, methyl-D-aspartate-binding, ionophore complexes;
aralkylamine compds. active at site on receptor-operated calcium
channels for treatment of neurol. disorders, and preparation of these
compds.)
IT Cytoprotective agents
(neuroprotectants, aralkylamine compds. active at site on
receptor-operated calcium channels for treatment of neurol. disorders,
and preparation of these compds.)
IT Receptors
(nicotinic, ionophore complexes; aralkylamine compds. active at site on
receptor-operated calcium channels for treatment of neurol. disorders,

and preparation of these compds.)

IT 170018-39-0P 170018-44-7P 170018-47-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 133805-32-0 144576-90-9 148920-48-3 170018-49-2
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 144451-98-9P 170018-46-9P 170018-54-9P 170018-55-0P 170018-57-2P
170018-63-0P 170018-68-5P 170018-71-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 5586-73-2 170018-40-3 170018-41-4 170018-42-5 170018-43-6
170018-45-8 170018-50-5 170018-51-6 170018-52-7 170018-53-8
170018-56-1 170018-58-3 170018-59-4 170018-60-7
170018-61-8 170018-62-9 170018-64-1 170018-70-9 170018-74-3
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 7440-70-2, Calcium, biological studies
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 14209-32-6P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 100-02-7, p-Nitrophenol, reactions 100-52-7, Benzaldehyde, reactions
107-13-1, 2-Propenenitrile, reactions 109-76-2, 1,3-Propanediamine
110-60-1, 1,4-Diaminobutane 135-02-4, o-Anisaldehyde 345-70-0,
3,3'-Difluorobenzophenone 456-48-4, 3-Fluorobenzaldehyde 462-94-2,
1,5-Pentanediamine 557-66-4, Ethylamine hydrochloride 587-04-2,
3-Chlorobenzaldehyde 1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1
5003-71-4 5460-29-7, N-(3-Bromopropyl)phthalimide 7300-34-7,
4,9-Dioxa-1,12-dodecanediamine 24424-99-5, Di-tert-butyl dicarbonate
99532-53-3 170019-09-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 455-67-4P 701-38-2P 4748-73-6P 38158-77-9P 51644-96-3P
75762-57-1P 83948-53-2P 101187-29-5P 105628-63-5P 114459-62-0P
122248-82-2P 122631-98-5P 122632-01-3P 122632-02-4P 128550-02-7P
128550-03-8P 128550-05-0P 128550-06-1P 144923-52-4P 147875-12-5P
147875-14-7P 147875-27-2P 170018-87-8P 170018-88-9P 170018-89-0P
170018-90-3P 170018-91-4P 170018-92-5P 170018-93-6P 170018-96-9P
170018-97-0P 170018-98-1P 170018-99-2P 170019-00-8P 170019-01-9P
170019-02-0P 170019-03-1P 170019-04-2P 170019-05-3P 170019-06-4P
170019-07-5P 170019-08-6P 170019-11-1P 170019-12-2P 170019-13-3P
170019-14-4P 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P
170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P
170019-24-6P 170019-25-7P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-95-8P 170019-10-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-66-3P 170018-67-4P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-48-1 170018-65-2 170018-69-6 **170018-72-1**
170018-73-2 **170018-75-4** 170018-76-5 170018-77-6
170018-78-7 170018-79-8 170018-80-1 170018-81-2 170018-82-3
170018-83-4 170018-84-5 170018-85-6 170018-86-7
(aralkylamine compds. active at site on receptor-operated calcium

channels for treatment of neurol. disorders, and preparation of these
compsds.)

L8 ANSWER 12 OF 22 USPATFULL on STN
ACCESSION NUMBER: 95:5942 USPATFULL
TITLE: 3,3-diphenylpropylamines and pharmaceutical
compositions thereof
INVENTOR(S): Jonsson, Nils A., Sodertalje, Sweden
Sparf, Bengt A., Tr.ang.ngsund, Sweden
Mikiver, Lembit, Jarna, Sweden
Moses, Pinchas, Saltsjo-Boo, Sweden
Nilvebrant, Lisbet, Bromma, Sweden
Glas, Gunilla, Sp.ang.nga, Sweden
PATENT ASSIGNEE(S): Pharmacia Aktiebolag, Uppsala, Sweden (non-U.S.
corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 5382600 | | 19950117 |
| APPLICATION INFO.: | US 1991-810185 | | 19911219 (7) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1990-543767, filed on 24 Sep 1990, now abandoned | | |

| | NUMBER | DATE |
|-----------------------|-------------------------------|----------|
| PRIORITY INFORMATION: | SE 1988-2076 | 19880122 |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Raymond, Richard L. | |
| LEGAL REPRESENTATIVE: | Pollock, Vande Sande & Priddy | |
| NUMBER OF CLAIMS: | 7 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1742 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Adrenergic antagonists
IT Antihistaminics
IT Cholinergic antagonists
(diphenylpropylamines)
IT Ion channel blockers
(calcium, diphenylpropylamines)
IT 51-41-2, Noradrenaline
(antagonists of, phenylpropylamines as)
IT 834-14-0P 883-90-9P 33921-65-2P 57322-71-1P 71238-52-3P
71238-54-5P 103849-16-7P 117896-34-1P 124937-55-9P 124937-56-0P
124937-57-1P 124937-58-2P 124937-59-3P 124937-60-6P 124937-61-7P
124937-62-8P 124937-63-9P 124937-64-0P 124937-65-1P 124937-66-2P
124937-67-3P 124937-68-4P 124937-69-5P 124937-70-8P 124937-71-9P
124937-72-0P 124937-73-1P 124937-74-2P 124937-75-3P 124937-76-4P
124937-77-5P 124937-78-6P 124937-79-7P 124937-80-0P 124937-81-1P
124937-82-2P 124937-83-3P 124937-84-4P 124937-85-5P 124937-86-6P
124937-87-7P 124937-88-8P 124937-89-9P 124937-90-2P 124937-91-3P
124937-92-4P 124937-93-5P 124937-94-6P 124937-95-7P 124937-96-8P
124937-97-9P 124937-98-0P 124938-02-9P 124938-03-0P 124938-04-1P
124938-05-2P 124938-06-3P 124938-07-4P 124938-08-5P 124938-09-6P
124938-10-9P 124977-70-4P
(preparation and reaction of, in preparation of drug)
IT 124935-86-0P 124935-87-1P 124935-88-2P 124935-89-3P 124935-90-6P
124935-91-7P 124935-92-8P 124935-93-9P 124935-94-0P 124935-95-1P
124935-96-2P 124935-97-3P 124935-98-4P 124935-99-5P 124936-00-1P
124936-01-2P 124936-02-3P 124936-03-4P 124936-04-5P 124936-05-6P
124936-06-7P 124936-07-8P 124936-08-9P 124936-09-0P 124936-10-3P
124936-11-4P 124936-12-5P 124936-13-6P **124936-14-7P**
124936-15-8P 124936-16-9P 124936-17-0P **124936-18-1P**
124936-19-2P 124936-20-5P 124936-21-6P 124936-22-7P
124936-23-8P 124936-24-9P 124936-25-0P 124936-26-1P 124936-27-2P
124936-28-3P 124936-29-4P 124936-30-7P 124936-31-8P
124936-32-9P 124936-33-0P 124936-34-1P
124936-35-2P 124936-36-3P 124936-37-4P

| | | | | |
|---|--------------|--------------|--------------|--------------|
| 124936-38-5P | 124936-39-6P | 124936-40-9P | 124936-41-0P | 124936-42-1P |
| 124936-43-2P | 124936-44-3P | 124936-45-4P | 124936-46-5P | 124936-47-6P |
| 124936-48-7P | 124936-49-8P | 124936-50-1P | 124936-51-2P | 124936-52-3P |
| 124936-53-4P | 124936-54-5P | 124936-55-6P | 124936-56-7P | 124936-57-8P |
| 124936-58-9P | 124936-59-0P | 124936-60-3P | 124936-61-4P | 124936-62-5P |
| 124936-63-6P | 124936-64-7P | 124936-65-8P | 124936-66-9P | 124936-67-0P |
| 124936-68-1P | 124936-69-2P | 124936-70-5P | 124936-71-6P | 124936-72-7P |
| 124936-73-8P | 124936-74-9P | 124936-75-0P | 124936-76-1P | 124936-77-2P |
| 124936-78-3P | 124936-79-4P | 124936-80-7P | 124936-81-8P | 124936-82-9P |
| 124936-83-0P | 124936-84-1P | 124936-85-2P | 124936-86-3P | 124936-87-4P |
| 124936-88-5P | 124936-89-6P | 124936-90-9P | 124936-91-0P | 124936-92-1P |
| 124936-93-2P | 124936-94-3P | 124936-95-4P | 124936-96-5P | 124936-97-6P |
| 124936-98-7P | 124936-99-8P | 124937-00-4P | 124937-01-5P | 124937-02-6P |
| 124937-03-7P | 124937-04-8P | 124937-05-9P | 124937-06-0P | 124937-07-1P |
| 124937-08-2P | 124937-09-3P | 124937-10-6P | 124937-11-7P | 124937-12-8P |
| 124937-13-9P | 124937-14-0P | 124937-15-1P | 124937-16-2P | 124937-17-3P |
| 124937-18-4P | 124937-19-5P | 124937-20-8P | 124937-21-9P | 124937-22-0P |
| 124937-23-1P | 124937-24-2P | 124937-25-3P | 124937-26-4P | 124937-27-5P |
| 124937-28-6P | 124937-29-7P | 124937-30-0P | 124937-31-1P | 124937-32-2P |
| 124937-33-3P 124937-34-4P 124937-35-5P | | | | |
| 124937-36-6P | 124937-37-7P | 124937-38-8P | 124937-39-9P | |
| 124937-40-2P | 124937-41-3P | 124937-42-4P | 124937-43-5P | 124937-44-6P |
| 124937-45-7P | 124937-46-8P | 124937-47-9P | 124937-48-0P | 124937-49-1P |
| 124937-50-4P | 124937-51-5P | 124937-52-6P | 124937-54-8P | 124938-01-8P |

(preparation of, as drug, especially anticholinergic)

IT 100-66-3, Anisole, reactions 103-36-6, Ethyl cinnamate 106-44-5,
reactions 106-48-9, p-Chlorophenol 108-39-4, reactions 108-95-2,
Phenol, reactions 123-31-9, 1,4-Benzenediol, reactions 124-68-5,
2-Amino-2-methylpropanol 151-10-0 459-57-4, p-Fluorobenzaldehyde
578-57-4, o-Bromoanisole 621-82-9, Cinnamic acid, reactions 768-66-1,
2,2,6,6-Tetramethylpiperidine 768-94-5, 1-Aminoadamantane 2403-88-5,
4-Hydroxy-2,2,6,6-tetramethylpiperidine 4567-22-0, 2,2,5,5-
Tetramethylpyrrolidine 6099-03-2, 2-Methoxycinnamic acid 7020-80-6
15854-55-4, Methyl 2,4-dimethoxycinnamate 15854-58-7, Methyl
2-methoxycinnamate 25855-75-8, 2,6-Dimethoxybenzophenone 40546-94-9
51737-00-9, 4-Phenyl-3,4-dihydrocoumarin 53005-58-6,
2-Methoxy-4-methylcinnamic acid 73108-72-2 88407-29-8 103986-76-1,
2-Methoxy-5-methylcinnamic acid 109089-77-2 124936-70-5 124937-13-9
124937-99-1 124938-00-7

(reaction of, in preparation of drug)

L8 ANSWER 13 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2000:70898 USPATFULL

TITLE: Compounds active at a novel site on receptor-operated
calcium channels useful for treatment of neurological
disorders and diseases

INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, United States
Balandrin, Manuel F., Sandy, UT, United States
VanWagenen, Bradford C., Salt Lake City, UT, United
States

DelMar, Eric G., Salt Lake City, UT, United States
Moe, Scott T., Salt Lake City, UT, United States
Artman, Linda D., Salt Lake City, UT, United States
Barmore, Robert M., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United
States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|-------|--------------|
| | ----- | ----- | ----- |
| PATENT INFORMATION: | US 6071970 | | 20000606 |
| APPLICATION INFO.: | US 1995-485038 | | 19950607 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. WO 1994-US12293, filed on 26 Oct 1994 which is a continuation-in-part of Ser. No. US 1994-288668, filed on 9 Aug 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-194210, filed on 8 Feb 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-14813, filed on 8 Feb 1993, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |

FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: Lyon & Lyon LLP
NUMBER OF CLAIMS: 185
EXEMPLARY CLAIM: 1
LINE COUNT: 5430

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method and compositions for treating a patient having a neurological disease or disorder, such as stroke, head trauma, spinal cord injury, epilepsy, anxiety, or neurodegenerative diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's Disease, or amyotrophic lateral sclerosis (ALS).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Ionophores
(NMDA receptor complex; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT Glutamate receptors
(NMDA-binding, ionophore complex; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT Nervous system
(degeneration, treatment; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT Cytoprotective agents
(neuroprotectants; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT Calcium channel
(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 5586-73-2P 28075-29-8P 90531-05-8P 133805-32-0P 144451-98-9P
144452-04-0P 144576-90-9P 148920-48-3P 170018-48-1P 170018-49-2P
170018-50-5P 170018-51-6P 170018-52-7P 170018-54-9P 170018-55-0P
170018-56-1P 170018-57-2P 170018-63-0P 170018-66-3P
170018-67-4P 170018-68-5P 170018-71-0P **170018-72-1P**
170018-73-2P 170018-74-3P **170018-75-4P** 170018-76-5P
170018-77-6P 170018-78-7P 170018-79-8P 170018-80-1P 170018-81-2P
170018-82-3P 170018-83-4P 170018-84-5P 170018-85-6P 170018-86-7P
170019-10-0P 186495-37-4P 186495-38-5P 186495-39-6P 186495-40-9P
186495-41-0P **186495-43-2P** **186495-44-3P** 186495-45-4P
186495-46-5P 186495-47-6P **186495-48-7P** 186495-49-8P
186495-50-1P 186495-51-2P 186495-53-4P 186495-54-5P 186495-56-7P
186495-93-2P **186495-94-3P** 186495-95-4P 186495-97-6P
186495-98-7P 186495-99-8P 186496-00-4P 186496-02-6P
186496-03-7P 200430-18-8P 217658-89-4P 217658-94-1P 217658-96-3P
217659-01-3P 217659-23-9P 217660-61-2P 273409-48-6P 273409-49-7P
273409-50-0P 273409-51-1P 273409-52-2P 273409-53-3P
(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 62-23-7, p-Nitrobenzoic acid 85-41-6, Phthalimide 100-52-7,
Benzaldehyde, reactions 105-34-0, Methyl cyanoacetate 107-13-1,
2-Propenenitrile, reactions 109-76-2, 1,3-Diaminopropane 110-60-1,
1,4-Diaminobutane 135-02-4, o-Anisaldehyde 285-67-6, Cyclopentene
oxide 345-70-0, 3,3'-Difluorobenzophenone 443-73-2,
5-Fluoroindole-3-acetic acid 452-08-4, 2-Bromo-4-fluoroanisole
456-48-4, 3-Fluorobenzaldehyde 462-94-2, 1,5-Diaminopentane 529-20-4,
2-Methylbenzaldehyde 546-68-9 578-57-4, 2-Bromoanisole 587-04-2,
3-Chlorobenzaldehyde 932-31-0, 2-Methylphenylmagnesium bromide
1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1 5003-71-4 5460-29-7,
N-(3-Bromopropyl)phthalimide 7300-34-7, 4,9-Dioxa-1,12-dodecandiamine
17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2,
(S)-N-Benzyl- α -methylbenzylamine 50715-13-4 65416-24-2, Benzyl
crotonate 77532-79-7, 5-Fluoro-2-methylbenzonitrile 122630-41-5
147624-13-3, 3-Fluoro-2-methylbenzaldehyde 168080-76-0,
3-Fluoro-2-methylbenzoyl chloride 263355-05-1, 3-Fluoro-2-
methylphenylmagnesium bromide
(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 455-67-4P 701-38-2P 4748-73-6P 14209-32-6P 35513-93-0P
38158-77-9P 51644-96-3P 75762-57-1P 83948-53-2P 98586-06-2P

| | | | | |
|--------------|---------------------|--------------|--------------|--------------|
| 101187-29-5P | 114459-62-0P | 122248-82-2P | 122631-98-5P | 122632-01-3P |
| 122632-02-4P | 128550-02-7P | 128550-03-8P | 128550-05-0P | 128550-06-1P |
| 128550-07-2P | 144923-52-4P | 147875-12-5P | 147875-14-7P | 170018-87-8P |
| 170018-88-9P | 170018-89-0P | 170018-90-3P | 170018-92-5P | 170018-96-9P |
| 170018-97-0P | 170019-07-5P | 170019-09-7P | 170019-11-1P | 170019-14-4P |
| 170019-15-5P | 170019-16-6P | 170019-17-7P | 170019-18-8P | 170019-19-9P |
| 170019-20-2P | 170019-21-3P | 170019-22-4P | 170019-23-5P | 170019-24-6P |
| 170019-25-7P | 186496-31-1P | 186496-32-2P | 186496-33-3P | 186496-34-4P |
| 186496-35-5P | 186496-36-6P | 186496-37-7P | 186496-38-8P | 186496-39-9P |
| 186496-40-2P | 186496-41-3P | 186496-42-4P | 186496-44-6P | 186496-45-7P |
| 186496-46-8P | 186496-48-0P | 186496-51-5P | 186496-52-6P | |
| 186496-53-7P | 273409-54-4P | 273409-55-5P | 273409-56-6P | 273409-57-7P |
| 273409-58-8P | 273409-62-4P | | | |

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

L8 ANSWER 14 OF 22 USPATFULL on STN

ACCESSION NUMBER: 76:58475 USPATFULL

TITLE: 1,4-Oxazepines as **antidepressant** agents

INVENTOR(S): Bowman, Robert Mathews, Summit, NJ, United States

PATENT ASSIGNEE(S): Ciba-Geigy Corporation, Ardsley, NY, United States
(U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 3988448 | | 19761026 |
| APPLICATION INFO.: | US 1974-526758 | | 19741125 (5) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Thomas, Jr., James O. | | |
| ASSISTANT EXAMINER: | Robinson, Allen J. | | |
| LEGAL REPRESENTATIVE: | Kolodny, Joseph G., Groeger, Theodore O., Maitner, John J. | | |
| NUMBER OF CLAIMS: | 4 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 753 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB 7,7-Diphenyl-hexahydro-1,4-oxazepines, e.g. those of the formula:
##SPC1##

Acyl derivatives, N-oxides and salts thereof are **antidepressants**

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Antidepressants
(hexahydrodiphenyloxazepines)

IT 4023-34-1
(acylation of (aminodiphenylpropoxy)acetaldehyde diethyl acetal)

IT 79-04-9
(acylation of benzylhydroxydiphenylpropylamines by)

IT 60163-68-0 60163-69-1 60163-70-4 60163-71-5 60280-67-3
(alkylation of)

IT 75-21-8, reactions 106-95-6 107-13-1, reactions 107-14-2
3874-54-2
(alkylation of diphenylhexahydrooxazepines by)

IT 98-88-4
(benzoylation of hydroxydiphenylpropylamines by)

IT 60163-58-8
(condensation with formaldehyde and reduction)

IT 100-52-7, reactions
(condensation with hydroxydiphenylpropylamine)

IT 60163-67-9
(cyclization of)

IT 60163-40-8P 60163-41-9P 60163-42-0P 60163-43-1P 60163-44-2P
60163-46-4P
(preparation and N-chloroacetylation of)

IT 60163-65-7P
(preparation and allylation of)

IT 50775-34-3P 60163-33-9P 60163-34-0P 60163-35-1P 60163-36-2P

60163-60-2P
(preparation and benzylation of)

IT 60163-61-3P
(preparation and chloroacetylation of)

IT 60162-88-1P
(preparation and chloroformylation of)

IT 60163-47-5P 60163-48-6P 60163-49-7P 60163-50-0P 60163-51-1P
60163-52-2P 60163-62-4P
(preparation and cyclization of)

IT 60163-45-3P 60163-64-6P
(preparation and hydrogenolysis of)

IT 3531-23-5P 4320-44-9P 60163-56-6P
(preparation and reactions of)

IT 50775-33-2P 60162-89-2P 60162-90-5P 60162-91-6P 60162-92-7P
60162-93-8P 60163-16-8P 60163-21-5P 60163-29-3P 60163-30-6P
60163-31-7P 60163-32-8P 60163-37-3P **60163-38-4P**
60163-39-5P 60163-53-3P 60163-55-5P 60163-59-9P 60163-60-2P
60163-63-5P 60181-44-4P
(preparation and reduction of)

IT 60162-87-0P 60162-89-2P 60162-90-5P 60162-91-6P 60162-92-7P
60162-93-8P 60162-94-9P 60162-95-0P 60162-96-1P 60162-97-2P
60162-98-3P 60162-99-4P 60163-00-0P 60163-01-1P 60163-02-2P
60163-03-3P 60163-04-4P 60163-05-5P 60163-06-6P 60163-08-8P
60163-09-9P 60163-10-2P 60163-11-3P 60163-12-4P 60163-13-5P
60163-14-6P 60163-15-7P 60163-17-9P 60163-18-0P 60163-19-1P
60163-20-4P 60163-22-6P 60163-23-7P 60163-25-9P 60163-26-0P
60163-27-1P 60163-28-2P 60163-57-7P
(preparation of)

IT 345-92-6 1016-78-0 2553-04-0 6136-67-0 54589-41-2 55363-58-1
(reaction of, with acetonitrile)

IT 541-41-3
(reaction of, with benzyldiphenylhexahydrooxazepine)

IT 51806-20-3
(reaction of, with hydroxydiphenylpropionitriles)

IT 60163-54-4
(reactions of)

IT 60163-66-8
(reduction of)

IT 119-61-9, reactions
(with acetonitrile)

IT 75-05-8, reactions
(with benzophenones)

L8 ANSWER 15 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2000:47267 USPATFULL

TITLE: Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, United States
Balandrin, Manuel F., Sandy, UT, United States
Van Wagenen, Bradford C., Salt Lake City, UT, United States

DelMar, Eric G., Salt Lake City, UT, United States
Moe, Scott T., Salt Lake City, UT, United States
Artman, Linda D., Salt Lake City, UT, United States
Barmore, Robert M., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6051610 | | 20000418 |
| APPLICATION INFO.: | US 1999-252433 | | 19990218 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1995-485038, filed on 7 Jun 1995 which is a continuation-in-part of Ser. No. WO 1994-US12293, filed on 26 Oct 1994 which is a continuation-in-part of Ser. No. US 1994-288668, filed on 9 Aug 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-194210, filed | | |

on 8 Feb 1994, now abandoned which is a
continuation-in-part of Ser. No. US 1993-14813, filed
on 8 Feb 1993, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: Lyon & Lyon LLP
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 4670

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Method and compositions for treating a patient having a neurological disease or disorder, such as stroke, head trauma, spinal cord injury, epilepsy, anxiety, or neurodegenerative diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's Disease, or amyotrophic lateral sclerosis (ALS).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Analgesics
IT Anticonvulsants and Antiepileptics
IT Anxiolytics
IT Muscle relaxants
IT Nervous system agents
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Amines, biological studies
(aralkyl, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Ion channel
(calcium, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Anesthetics
(general, adjuncts; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
(glutamatergic, AMPA-binding, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
(glutamatergic, kainate-binding, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
(glutamatergic, methyl-D-aspartate-binding, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Cytoprotective agents
(neuroprotectants, aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT Receptors
(nicotinic, ionophore complexes; aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 170018-39-0P 170018-44-7P 170018-47-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)
IT 133805-32-0 144576-90-9 148920-48-3 170018-49-2
(aralkylamine compds. active at site on receptor-operated calcium

channels for treatment of neurol. disorders, and preparation of these compds.)

IT 144451-98-9P 170018-46-9P 170018-54-9P 170018-55-0P 170018-57-2P
170018-63-0P 170018-68-5P 170018-71-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 5586-73-2 170018-40-3 170018-41-4 170018-42-5 170018-43-6
170018-45-8 170018-50-5 170018-51-6 170018-52-7 170018-53-8
170018-56-1 170018-58-3 170018-59-4 170018-60-7
170018-61-8 170018-62-9 170018-64-1 170018-70-9 170018-74-3
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 7440-70-2, Calcium, biological studies
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 14209-32-6P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 100-02-7, p-Nitrophenol, reactions 100-52-7, Benzaldehyde, reactions
107-13-1, 2-Propenenitrile, reactions 109-76-2, 1,3-Propanediamine
110-60-1, 1,4-Diaminobutane 135-02-4, o-Anisaldehyde 345-70-0,
3,3'-Difluorobenzophenone 456-48-4, 3-Fluorobenzaldehyde 462-94-2,
1,5-Pentanediamine 557-66-4, Ethylamine hydrochloride 587-04-2,
3-Chlorobenzaldehyde 1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1
5003-71-4 5460-29-7, N-(3-Bromopropyl)phthalimide 7300-34-7,
4,9-Dioxa-1,12-dodecanediamine 24424-99-5, Di-tert-butyl dicarbonate
99532-53-3 170019-09-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 455-67-4P 701-38-2P 4748-73-6P 38158-77-9P 51644-96-3P
75762-57-1P 83948-53-2P 101187-29-5P 105628-63-5P 114459-62-0P
122248-82-2P 122631-98-5P 122632-01-3P 122632-02-4P 128550-02-7P
128550-03-8P 128550-05-0P 128550-06-1P 144923-52-4P 147875-12-5P
147875-14-7P 147875-27-2P 170018-87-8P 170018-88-9P 170018-89-0P
170018-90-3P 170018-91-4P 170018-92-5P 170018-93-6P 170018-96-9P
170018-97-0P 170018-98-1P 170018-99-2P 170019-00-8P 170019-01-9P
170019-02-0P 170019-03-1P 170019-04-2P 170019-05-3P 170019-06-4P
170019-07-5P 170019-08-6P 170019-11-1P 170019-12-2P 170019-13-3P
170019-14-4P 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P
170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P
170019-24-6P 170019-25-7P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-95-8P 170019-10-0P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-66-3P 170018-67-4P
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

IT 170018-48-1 170018-65-2 170018-69-6 **170018-72-1**
170018-73-2 **170018-75-4** 170018-76-5 170018-77-6
170018-78-7 170018-79-8 170018-80-1 170018-81-2 170018-82-3
170018-83-4 170018-84-5 170018-85-6 170018-86-7
(aralkylamine compds. active at site on receptor-operated calcium channels for treatment of neurol. disorders, and preparation of these compds.)

L8 ANSWER 16 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2005:324947 USPATFULL

TITLE: Dual acting SNRI-NMDA antagonists for the treatment of genitourinary disorders

INVENTOR(S): Thor, Karl Bruce, Cary, NC, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2005282859 | A1 | 20051222 |
| APPLICATION INFO.: | US 2005-145022 | A1 | 20050603 (11) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2004-576999P | 20040604 (60) |
| | US 2004-607820P | 20040907 (60) |
| | US 2004-640105P | 20041228 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109, US | |
| NUMBER OF CLAIMS: | 92 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 6 Drawing Page(s) | |
| LINE COUNT: | 4912 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are compositions and methods for treatment of genitourinary disorders (e.g., urge incontinence). The compositions may generally include a dual-acting SNRI-NMDA antagonist (e.g., bicifadine and/or milnacipran). Alternatively, the compositions may generally include an SNRI and an NMDA antagonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Disease, animal
(Fowler's syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Glutamate antagonists
(NMDA antagonists; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Prostate gland, disease
(benign hyperplasia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Hyperplasia
(benign prostatic; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(buccal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(capsules; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Pain
(chronic pelvic pain syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(controlled-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease

IT Inflammation
(cystitis, interstitial (cell); dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(delayed release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra
(disease, urethritis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT 5-HT reuptake inhibitors

IT Analgesics

IT Anti-inflammatory agents

IT Antitumor agents

IT Bladder, disease

IT Combination chemotherapy
IT Drug delivery systems
IT Human
IT Neoplasm
IT Urogenital system, disease
 (dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
IT Bladder, disease
 (hyperreflexia; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Bladder, disease
 (incontinence; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (inhalants; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (intravesical; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (mucosal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
IT Nervous system agents
 (noradrenaline reuptake inhibitors; dual-acting serotonin-
 norepinephrine reuptake inhibitor-NMDA antagonists for treatment of
 genitourinary disorders)
IT Drug delivery systems
 (oral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
IT Testis
 (orchialgia; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Bladder, disease
 (overactive bladder, including overactive bladder with sphincter
 dysfunction; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Disease, animal
 (pelvic hypersensitivity or sphincteric spasticity; dual-acting
 serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for
 treatment of genitourinary disorders)
IT Prostate gland, disease
 (prostodynia; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Inflammation
IT Prostate gland, disease
 (prostatitis; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (pulsatile-release; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (rectal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
IT Bladder
 (smooth muscle; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Muscle
 (smooth, urinary bladder; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (sublingual; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (sustained-release; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT Drug delivery systems
 (tablets; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
IT Drug delivery systems

(transdermal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(transurethral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra
(urethra stricture disease; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Inflammation
(urethritis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Reproductive system
(vulva, vulvodynia or vulvar vestibulitis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT 5586-73-2 14451-09-3, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
21745-77-7, 9H-Xanthene-9-ethanamine 21745-81-3, 9H-Thioxanthene-9-ethanamine 21745-82-4 21745-85-7 28075-29-8 57226-64-9
63106-93-4 63940-51-2 66504-40-3 69096-48-6 71195-57-8
92623-85-3 105310-27-8 109306-10-7 136090-96-5 136090-97-6
144451-98-9 153275-06-0 170018-66-3 170018-67-4 170018-79-8
170018-83-4 186495-47-6 **186495-48-7** 186495-49-8
186495-52-3 186495-53-4 186495-54-5 186495-55-6 186495-56-7
186495-66-9 186495-67-0 186495-80-7 186495-84-1 186495-86-3
186495-87-4 186495-88-5 186495-89-6 186495-90-9 186496-20-8
186496-23-1 186496-29-7 186496-30-0 186496-71-9 200429-73-8
200429-74-9 200429-75-0 200429-79-4 200429-80-7 200429-81-8
200429-82-9 200429-83-0 200429-84-1 200429-85-2 200429-86-3
200429-87-4 255039-66-8 255039-67-9 255039-68-0 255039-69-1
255039-71-5 255039-73-7 255039-75-9 255039-77-1 255039-79-3
255039-81-7 255040-00-7 255040-01-8 255040-02-9 255040-03-0
255040-04-1 255040-05-2 255040-07-4 255040-08-5 410074-73-6
410074-75-8 435293-68-8 688738-11-6 688738-12-7 871100-17-3
871100-18-4 871100-19-5 871100-20-8 871100-21-9 871100-22-0
871100-23-1 871331-21-4 871331-22-5 871331-23-6 871331-24-7
871331-25-8
(dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

L8 ANSWER 17 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2000:1911 USPATFULL
TITLE: Calcium receptor-active molecules
INVENTOR(S): Nemeth, Edward F., Salt Lake City, UT, United States
Van Wagenen, Bradford C., Salt Lake City, UT, United States
Balandrin, Manuel F., Sandy, UT, United States
DelMar, Eric G., Salt Lake City, UT, United States
Moe, Scott T., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)
The Brigham and Women's Hospital, Boston, MA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6011068 | | 20000104 |
| APPLICATION INFO.: | US 1994-353784 | | 19941208 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. WO 1994-US12117, filed on 21 Oct 1994 And a continuation-in-part of Ser. No. US 1994-292827, filed on 19 Aug 1994, now abandoned And a continuation-in-part of Ser. No. US 1993-141248, filed on 22 Oct 1993, now abandoned And a continuation-in-part of Ser. No. US 1993-9389, filed on 23 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17127, filed on 12 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-934161, filed on 21 Aug 1992, now abandoned which is a | | |

continuation-in-part of Ser. No. US 1992-834044, filed
on 11 Feb 1992, now abandoned which is a
continuation-in-part of Ser. No. US 1991-749451, filed
on 23 Aug 1991, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Henley, III, Raymond
LEGAL REPRESENTATIVE: Lyon & Lyon LLP
NUMBER OF CLAIMS: 103
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 111 Drawing Figure(s); 85 Drawing Page(s)
LINE COUNT: 7466

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the different roles inorganic ion receptors have in cellular and body processes. The present invention features: (1) molecules which can modulate one or more inorganic ion receptor activities, preferably the molecule can mimic or block an effect of an extracellular ion on a cell having an inorganic ion receptor, more preferably the extracellular ion is Ca^{2+} and the effect is on a cell having a calcium receptor; (2) inorganic ion receptor proteins and fragments thereof, preferably calcium receptor proteins and fragments thereof; (3) nucleic acids encoding inorganic ion receptor proteins and fragments thereof, preferably calcium receptor proteins and fragments thereof; (4) antibodies and fragments thereof, targeted to inorganic ion receptor proteins, preferably calcium receptor protein; and (5) uses of such molecules, proteins, nucleic acids and antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Animal cell line
(CHO; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Animal cell line
(Hek 293; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Structure-activity relationship
(calcium-modulating; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Ion channel blockers
(calcium; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Resolution (separation)
(chromatog.; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT cDNA sequences
(for mammalian calcium receptors)

IT Drug delivery systems

IT Drug screening

IT Osteoclast
(ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Protamines
(ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT mRNA
(ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Thyroid gland, neoplasm
(medullary carcinoma, rMTC 6-23 cell; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Protein sequences
(of mammalian calcium receptors)

IT Egg

(oocyte, *Xenopus*; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT *Xenopus*
(oocyte; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Osteoclast
(osteoclastoma; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Parathyroid gland
(parathyroid cell; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Hyperparathyroidism
(secondary; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT Antibodies
(to calcium receptors; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 153834-08-3 161663-06-5 168183-63-9 168257-64-5
(amino acid sequence; ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 7439-91-0, Lanthanum, biological studies 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies 7440-54-2, Gadolinium, biological studies 16561-29-8, Phorbol myristate acetate 35094-46-3
(ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 148717-47-9P, NPS-467 148717-56-0P, NPS R-467 148740-52-7P, NPS S-467
(ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 148717-54-8P, NPS R-568 179381-53-4P 179381-55-6P 179381-59-0P 179381-61-4P 179381-63-6P 179381-65-8P 179381-66-9P 179381-68-1P 252055-41-7P 253337-73-4P
(ion receptor- and calcium receptor-active mols., receptor proteins, nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 57-92-1, biological studies 71-44-3, Spermine 112-24-3 112-57-2, Tetraethylenepentamine 119-04-0, Neomycin B 124-20-9, Spermidine 296-35-5, Hexacyclen 390-64-7, Prenylamine 1403-66-3, Gentamicin 1404-04-2, Neomycin 2783-17-7, 1,12-Dodecanediamine 4067-16-7, Pentaethylenehexamine 4696-76-8, Bekanamycin 13042-18-7, Fendiline 15834-81-8 24937-47-1, Polyarginine 25104-18-1, Polylysine 25212-18-4, Polyarginine 33542-87-9 38000-06-5, Polylysine 38235-77-7 85610-72-6 87955-89-3, NPS 383 95956-62-0 108393-62-0 108448-58-4 111944-83-3, Argiotoxin 659 114753-78-5 125275-99-2 128549-96-2, NPS 017 128549-97-3, NPS 015 133805-32-0, NPS 019 148717-47-9D, complexes 148717-48-0 148717-49-1 148717-49-1D, complexes 148717-51-5, NPS 382 148717-53-7 148717-54-8D, complexes 148717-56-0D, complexes 148740-50-5, NPS 381 148740-51-6, NPS 021 159149-49-2 159149-51-6 159149-75-4, NPS S-568 159149-76-5 159149-76-5D, complexes 159149-93-6 159149-96-9 159149-96-9D, complexes 159149-97-0 159149-97-0D, complexes 159150-00-2 159150-00-2D, complexes **159150-01-3** 159150-03-5 159150-03-5D, complexes 159150-04-6 159150-04-6D, complexes 159150-05-7 159150-05-7D, complexes 159150-06-8 159150-06-8D, complexes 159150-17-1 159150-18-2 159150-18-2D, complexes 159150-19-3 159150-19-3D, complexes 159150-20-6 159150-20-6D, complexes 159150-28-4 159150-28-4D, complexes 159150-29-5 159150-29-5D, complexes 159150-30-8 165304-87-0 165304-87-0D, complexes 179381-56-7 179381-56-7D, complexes 179381-62-5 179381-62-5D, complexes 179381-64-7 179381-64-7D, complexes 179381-67-0 179381-67-0D, complexes 179381-69-2 179381-69-2D, complexes 179381-70-5 179381-70-5D, complexes 179381-74-9 179381-74-9D, complexes 179381-75-0 179381-75-0D, complexes

179381-86-3 179381-86-3D, complexes 179603-34-0 179603-34-0D,
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 179603-37-3D, complexes 179603-38-4 179603-38-4D, complexes
 179603-41-9 179603-41-9D, complexes 179603-42-0 179603-42-0D,
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 199615-27-5D, complexes 199615-28-6 199615-28-6D, complexes
 199615-34-4 199615-34-4D, complexes 199734-44-6 199734-45-7
 199734-46-8 219686-00-7 219686-00-7D, complexes 219686-01-8
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 253337-10-9 253337-10-9D, complexes 253337-11-0 253337-11-0D,
 complexes 253337-12-1 253337-12-1D, complexes 253337-13-2
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 complexes 253337-22-3 253337-22-3D, complexes 253337-23-4
 253337-23-4D, complexes 253337-24-5 253337-24-5D, complexes
 253337-26-7 253337-26-7D, complexes

(ion receptor- and calcium receptor-active mols., receptor proteins,
 nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 253337-27-8 253337-27-8D, complexes 253337-28-9 253337-28-9D,
 complexes 253337-29-0 253337-29-0D, complexes 253337-30-3
 253337-30-3D, complexes 253337-32-5 253337-32-5D, complexes
 253337-33-6 253337-33-6D, complexes 253337-34-7 253337-34-7D,
 complexes 253337-35-8 253337-35-8D, complexes 253337-36-9
 253337-36-9D, complexes 253337-37-0 253337-37-0D, complexes
 253337-38-1 253337-38-1D, complexes 253337-39-2 253337-39-2D,
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 253337-41-6D, complexes 253337-42-7 253337-42-7D, complexes
 253337-43-8 253337-43-8D, complexes 253337-44-9 253337-44-9D,
 complexes 253337-45-0 253337-45-0D, complexes 253337-46-1
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 253337-49-4 253337-49-4D, complexes 253337-50-7 253337-50-7D,
 complexes 253337-51-8 253337-51-8D, complexes 253337-52-9
 253337-52-9D, complexes 253337-53-0 253337-53-0D, complexes
 253337-54-1 253337-54-1D, complexes 253337-55-2 253337-55-2D,
 complexes 253337-56-3 253337-56-3D, complexes 253337-57-4
 253337-57-4D, complexes 253337-58-5 253337-58-5D, complexes
 253337-59-6 253337-59-6D, complexes 253337-60-9 253337-60-9D,
 complexes 253337-61-0 253337-61-0D, complexes 253337-62-1
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 253337-64-3 253337-64-3D, complexes 253337-65-4 253337-65-4D,
 complexes 253337-66-5 253337-66-5D, complexes

(ion receptor- and calcium receptor-active mols., receptor proteins,
 nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 60-92-4, Cyclic AMP 7440-70-2, Calcium, biological studies 9002-64-6,

Parathyroid hormone 9007-12-9, Calcitonin 16887-00-6, Chloride,
biological studies 27121-73-9, Inositol triphosphate 105182-27-2,
Inositol monophosphate

(ion receptor- and calcium receptor-active mols., receptor proteins,
nucleic acids encoding them, anti-receptor antibodies, and uses)

IT 153834-07-2 161048-76-6 163874-32-6 163874-33-7

(nucleotide sequence; ion receptor- and calcium receptor-active mols.,
receptor proteins, nucleic acids encoding them, anti-receptor
antibodies, and uses)

IT 1441-99-2P, 3'-Thiomethylacetophenone 10024-90-5P 37612-52-5P
124829-12-5P

(preparation and reaction; ion receptor- and calcium receptor-active mols.,
receptor proteins, nucleic acids encoding them, anti-receptor
antibodies, and uses)

IT 93-08-3, 2'-Acetonaphthone 99-03-6, 3'-Aminoacetophenone 100-06-1,
4'-Methoxyacetophenone 122-03-2, 4-Isopropylbenzaldehyde 586-37-8,
3'-Methoxyacetophenone 876-02-8, 4'-Hydroxy-3'-methylacetophenone
941-98-0, 1'-Acetonaphthone 1504-74-1, 2-Methoxycinnamaldehyde
2038-57-5, 3-Phenylpropylamine 2420-16-8, 3-Chloro-4-
hydroxybenzaldehyde 3886-70-2 4903-09-7 5188-07-8, Sodium
thiomethoxide 18655-48-6 68376-32-9, 2-Methylcinnamionitrile
88196-70-7

(reaction; ion receptor- and calcium receptor-active mols., receptor
proteins, nucleic acids encoding them, anti-receptor antibodies, and
uses)

IT 206370-64-1, 10: PN: US6011068 SEQID: 1 unclaimed DNA 206370-65-2
206370-66-3 206370-67-4 206370-68-5, GenBank I75055 206370-69-6,
GenBank I75056 219676-88-7 219676-89-8 253834-47-8 253834-48-9
253835-22-2 253835-23-3

(unclaimed nucleotide sequence; ion receptor- and calcium
receptor-active mols., receptor proteins, nucleic acids encoding them,
anti-receptor antibodies, and uses)

IT 78005-41-1, Protamine CII (Oncorhynchus mykiss testis) 219686-07-4
219686-09-6 219686-11-0 219686-12-1 219686-13-2 219686-14-3
219686-15-4 219686-16-5

(unclaimed protein sequence; ion receptor- and calcium receptor-active
mols., receptor proteins, nucleic acids encoding them, anti-receptor
antibodies, and uses)

L8 ANSWER 18 OF 22 USPATFULL on STN

ACCESSION NUMBER: 1999:4350 USPATFULL

TITLE: Method of screening calcium receptor-active molecules

INVENTOR(S): Nemeth, Edward F., Salt Lake City, UT, United States

Brown, Edward M., Milton, MA, United States

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States

Van Wagenen, Bradford C., Salt Lake City, UT, United
States

Balandrin, Manuel F., Sandy, UT, United States

Del Mar, Eric G., Salt Lake City, UT, United States

PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., Boston, MA,
United States (U.S. corporation)

NPS Pharmaceuticals, Inc., Salt Lake City, UT, United
States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 5858684 | | 19990112 |
| APPLICATION INFO.: | US 1995-480751 | | 19950607 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1994-353784, filed on 8 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-292827, filed on 19 Aug 1994, now abandoned And a continuation-in-part of Ser. No. US 1993-141248, filed on 22 Oct 1993, now abandoned And a continuation-in-part of Ser. No. US 1993-9389, filed on 23 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-17127, filed on 12 Feb 1993, now abandoned which is a | | |

continuation-in-part of Ser. No. US 1992-934161, filed on 21 Aug 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-834044, filed on 11 Feb 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-749451, filed on 23 Aug 1991, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Sorensen, Kenneth A.
LEGAL REPRESENTATIVE: Lyon & Lyon LLP
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 111 Drawing Figure(s); 85 Drawing Page(s)
LINE COUNT: 7588

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the different roles inorganic ion receptors have in cellular and body processes. The present invention features: (1) molecules which can modulate one or more inorganic ion receptor activities, preferably the molecule can mimic or block an effect of an extracellular ion on a cell having an inorganic ion receptor, more preferably the extracellular ion is Ca^{2+} and the effect is on a cell having a calcium receptor; (2) inorganic ion receptor proteins and fragments thereof, preferably calcium receptor proteins and fragments thereof; (3) nucleic acids encoding inorganic ion receptor proteins and fragments thereof, preferably calcium receptor proteins and fragments thereof; (4) antibodies and fragments thereof, targeted to inorganic ion receptor proteins, preferably calcium receptor protein; and (5) uses of such molecules, proteins, nucleic acids and antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Plasmid vectors
(-471SportsCaRB, expression vector bovine calcium receptor cDNA; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Plasmid vectors
(CMV-BoPCaR, expression vector bovine calcium receptor cDNA; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Plasmid vectors
(CMVHuPCaR4.0, expression vector human calcium receptor cDNA; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Hyperparathyroidism
(calcium receptor effectors in treatment of models of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Parathyroid gland
(calcium receptor of, cloning and expression of gene for; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Receptors
(calcium, screening for calcimimetics and calcilytics; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Ion channel blockers
(calcium, screening for; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Structure-activity relationship
(calcium-mobilizing; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Osteoclast
(comps. acting on calcium receptors of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT PCR (polymerase chain reaction)

(degenerate, amplification of inorg. ion receptor cDNAs; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Primers (nucleic acid)
(for amplification of inorg. ion receptor cDNAs; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Receptors
(inorg. ion; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Pharmacology
(of calcium receptor subtypes; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Plasmid vectors
(pSV-BoPCaR, expression vector bovine calcium receptor cDNA; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Plasmid vectors
(pSV-HuPCaR4.0, expression vector human calcium receptor cDNA; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Plasmid vectors
(pSV-HuPCaR5.2, expression vector human calcium receptor cDNA; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Amines, biological studies
(phenylalkyl, effects on cytosolic calcium responses of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Amines, biological studies
(polyamines, nonpolymeric, mobilization of intracellular calcium by; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Antibodies
(to calcium and inorg. ion receptors; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT Drug screening
(whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT 128549-96-2, Agatoxin 489
(NPS 017, effects on C cell calcium receptor of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT 153834-08-3 168183-63-9 168257-64-5
(amino acid sequence; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT 161663-06-5
(amino acid sequence; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT 128549-97-3, Agatoxin 505 133805-32-0, NPS 019
(effects on C cell calcium receptor of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

IT 52-53-9, Verapamil 3193-62-2 13042-18-7, Fendiline 15834-81-8
16662-47-8, D-600 27790-75-6D, Dihydropyridine, analogs 33542-87-9
42399-41-7, Diltiazem 57818-92-5, TMB-8 85610-72-6, (-)-Prenylamine
95956-62-0 105029-41-2, Argiotoxin 636 108448-58-4, (-)-Fendiline
111944-83-3, Argiotoxin 659 114753-78-5 148717-47-9, NPS 467
148717-48-0 148717-49-1, NPS 568 148717-52-6, NPS 384 148717-53-7
148717-54-8, NPS R-568 148717-56-0, NPS R-467 148740-52-7, NPS S-467
159149-49-2 159149-51-6 159149-75-4, NPS S-568 159149-76-5
159149-93-6 159149-96-9 159149-97-0 159150-00-2 **159150-01-3**
159150-03-5 159150-04-6 159150-06-8 159150-17-1 159150-29-5
159150-30-8 179381-56-7 179603-38-4 179603-41-9 179603-42-0

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| | 199614-43-2 | 199614-44-3 | 199614-46-5 | 199614-48-7 | 199614-50-1 |
| | 199614-53-4 | 199614-55-6 | 199614-57-8 | 199614-61-4 | 199614-63-6 |
| | 199614-68-1 | 199614-82-9 | 199614-83-0 | 199614-84-1 | 199614-85-2 |
| | 199614-86-3 | 199614-87-4 | 199614-88-5 | 199614-89-6 | 199614-90-9 |
| | 199614-91-0 | 199614-92-1 | 199614-93-2 | 199614-94-3 | 199614-95-4 |
| | 199734-44-6 | 199734-45-7 | 199734-46-8 | 219685-99-1 | 219686-00-7 |
| | 219686-01-8 | 219686-02-9 | 219686-05-2 | | |
| | (effects on cytosolic calcium responses of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 159150-19-3P | 179381-60-3P | 179381-62-5P | 179381-64-7P | 179381-67-0P |
| | 179381-69-2P | 179381-75-0P | 199615-07-1P | | |
| | (effects on cytosolic calcium responses of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 148740-51-6, NPS 021 | | | | |
| | (effects on parathyroid calcium receptor of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 219686-07-4 | 219686-09-6 | 219686-11-0 | 219686-12-1 | 219686-13-2 |
| | 219686-14-3 | 219686-15-4 | 219686-16-5 | | |
| | (epitope of bovine parathyroid calcium receptor; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 74-88-4, Iodomethane, reactions 93-08-3 122-03-2, | | | | |
| | 4-Isopropylbenzaldehyde | 546-68-9 | 586-37-8 | 876-02-8 | 941-98-0, |
| | 1-Acetonaphthone | 1191-15-7, | Diisobutylaluminum hydride | 1504-74-1, | |
| | 2-Methoxycinnamaldehyde | 2038-57-5, | 3-Phenylpropylamine | 3886-70-2 | |
| | 5188-07-8, | Sodium thiomethoxide | 7315-17-5, | 2-Chlorohydrocinnamionitrile | |
| | 10024-90-5 | 18655-48-6 | 68376-32-9, | 2-Methylcinnamionitrile | 88196-70-7 |
| | (in synthesis of calcium channel effectors; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 9007-12-9, Calcitonin | | | | |
| | (induction of secretion of; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 57-92-1, Streptomycin, biological studies 71-44-3, Spermine 112-24-3, | | | | |
| | Triethylenetetramine | 112-57-2, | Tetraethylenepentamine | 124-20-9, | |
| | Spermidine | 296-35-5, | Hexacyclen | 1403-66-3, | Gentamycin 1404-04-2, |
| | Neomycin | 4067-16-7 | 4696-76-8, | Bekanamycin | 24937-47-1, |
| | Polyarginine | 25104-18-1, | Polylysine | 25212-18-4, | Polyarginine 38000-06-5, |
| | Polylysine | 78005-41-1, | Protamine CII (Oncorhynchus mykiss testis) | | |
| | 87955-89-3, | NPS 383 | 108820-26-4 | 148717-51-5, | NPS 382 148740-50-5, |
| | NPS 381 | | | | |
| | (mobilization of intracellular calcium by; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 153834-07-2, DNA (cattle clone BoPCaR-1 calcium receptor cDNA plus flanks) 206370-65-2 206370-66-3 206370-67-4 | | | | |
| | (nucleotide sequence; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 219686-08-5P | | | | |
| | (preparation and reactions in synthesis of calcium channel effectors; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 4903-09-7P, 3-Chloro-4-methoxybenzaldehyde 37612-52-5P 124829-13-6P | | | | |
| | (preparation and reactions of in synthesis of calcium channel effectors; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 219676-88-7 219676-89-8 219676-91-2 219676-92-3 | | | | |
| | (primer for amplification of inorg. ion receptor cDNAs; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |
| IT | 7440-70-2, Calcium, biological studies | | | | |
| | (receptor for, screening calcimimetics and calcilytics; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors) | | | | |

IT 9002-64-6, Parathormone
(secretion of, in testing of calcium receptor effectors; whole-cell assays and expression systems for calcium receptor genes and their use in screening for effectors of calcium receptors)

L8 ANSWER 19 OF 22 USPATFULL on STN

ACCESSION NUMBER: 1998:65348 USPATFULL
TITLE: Calcium receptor-active molecules
INVENTOR(S): Brown, Edward M., Milton, MA, United States
Hebert, Steven C., Wellesley, MA, United States
Garrett, Jr., James E., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc, Boston, MA, United States (U.S. corporation)
NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 5763569 | | 19980609 |
| APPLICATION INFO.: | US 1995-484565 | | 19950607 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1994-353784, filed on 8 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-292827, filed on 19 Aug 1994, now abandoned Ser. No. Ser. No. US 1993-141248, filed on 22 Oct 1993, now abandoned And Ser. No. US 1993-9389, filed on 23 Feb 1993, now abandoned , said Ser. No. US -292827 which is a continuation-in-part of Ser. No. US -141248 which is a continuation-in-part of Ser. No. US -9389 And a continuation-in-part of Ser. No. US 1993-17127, filed on 12 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-934161, filed on 21 Aug 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-834044, filed on 11 Feb 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-749451, filed on 23 Aug 1991, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Walsh, Stephen | | |
| ASSISTANT EXAMINER: | Sorensen, Kenneth A. | | |
| LEGAL REPRESENTATIVE: | Lyon & Lyon LLP | | |
| NUMBER OF CLAIMS: | 13 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 111 Drawing Figure(s); 85 Drawing Page(s) | | |
| LINE COUNT: | 6942 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention features calcium receptor polypeptides and fragments thereof. Uses of a calcium receptor polypeptide include providing a polypeptide having the activity of a calcium receptor polypeptide. Calcium receptor polypeptide fragments can be used, for example, to generate antibodies to a calcium receptor polypeptide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Thyroid gland
(C cell; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Antibiotics
(aminoglycoside; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Amines, biological studies
(aralkyl; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Ion channel blockers
(calcium; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy

of disorders of calcium metabolism)

IT Receptors
(calcium; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Drug screening

IT Hyperparathyroidism

IT Molecular cloning

IT Osteoclast

IT Osteoporosis

IT Parathyroid gland

IT Xenopus laevis
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Antibodies
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Protamines
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT cDNA sequences
(for calcium receptors from cattle and human and rat)

IT Protein sequences
(of calcium receptors from cattle and human and rat)

IT Secretion (process)
(of parathormone or calcitonin; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Egg
(oocyte, Xenopus; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Amines, biological studies
(polyamines, nonpolymeric; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 153834-08-3 161663-06-5 168183-63-9 168257-64-5
(amino acid sequence; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 159150-19-3P 179381-75-0P
(chemical syntheses of agonists/antagonists; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 93-08-3, 2'-Acetonaphthone 99-03-6, 3'-Aminoacetophenone 100-06-1, 4'-Methoxyacetophenone 122-03-2, 4-Isopropylbenzaldehyde 876-02-8, 4'-Hydroxy-3'-methylacetophenone 941-98-0, 1'-Acetonaphthone 1441-99-2, 3'-Thiomethylacetophenone 1504-74-1, 2-Methoxycinnamaldehyde 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 3886-70-2, (R)-(+)-1-(1-Naphthyl)ethylamine 4903-09-7 7315-17-5, 2-Chlorohydrocinnamionitrile 37612-52-5, 3'-Chloro-4'-methoxyacetophenone 68376-32-9, 2-Methylcinnamionitrile 88196-70-7
(chemical synthesis of agonists/antagonists; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 10024-90-5P 124829-13-6P
(chemical synthesis of agonists/antagonists; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 148717-54-8P, NPS R-568 179381-60-3P 179381-62-5P 179381-64-7P 179381-67-0P 179381-69-2P 199614-84-1P 199614-89-6P 199614-93-2P 199615-07-1P
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 52-53-9, Verapamil 57-92-1, Streptomycin, biological studies 71-44-3,

Spermine 112-24-3, Triethylenetetramine 112-57-2,
Tetraethylenepentamine 119-04-0, Neomycin B 124-20-9, Spermidine
296-35-5, Hexacyclen 1403-66-3, Gentamicin 2783-17-7,
1,12-Diaminododecane 4067-16-7, Pentaethylenehexamine 4696-76-8,
Beknamycin 7439-95-4, Magnesium, biological studies 13042-18-7,
Fendiline 15834-81-8 16662-47-8, D-600 24937-47-1, Polyarginine
25104-18-1, Polylysine 25212-18-4, Polyarginine 33542-87-9
38000-06-5, Polylysine 38235-77-7 38235-77-7D, substituted derivs.
42399-41-7, Diltiazem 57818-92-5, TMB-8 66469-40-7 66469-40-7D,
substituted derivs. 85610-72-6 87955-89-3, NPS 383 95956-62-0
105029-41-2, Argiotoxin-636 108393-62-0 108448-58-4, (-)-Fendiline
111944-83-3, Argiotoxin-659 128549-96-2, NPS 017 128549-97-3, NPS 015
133805-32-0, NPS 019 148717-48-0 148717-51-5 148717-52-6, NPS 384
148717-53-7 148717-56-0, NPS R-467 148740-50-5, NPS 381
148740-51-6, NPS 021 148740-52-7, NPS S-467 159149-49-2 159149-51-6
159149-75-4, NPS S-568 159149-76-5 159149-93-6 159149-96-9
159149-97-0 159150-00-2 **159150-01-3** 159150-03-5
159150-04-6 159150-06-8 159150-17-1 159150-29-5 159150-30-8
179381-56-7 179381-70-5 179381-74-9 179603-34-0 179603-37-3
179603-38-4 179603-41-9 179603-42-0 199614-29-4D, substituted
derivs. 199614-33-0 199614-43-2 199614-44-3 199614-46-5
199614-48-7 199614-50-1 199614-53-4 199614-55-6 199614-57-8
199614-61-4 199614-63-6 199614-68-1 199614-73-8 199614-76-1
199614-77-2 199614-78-3 199614-79-4 199614-80-7 199614-81-8
199614-82-9 199614-83-0 199614-85-2 199614-86-3 199614-87-4
199614-88-5 199614-90-9 199614-91-0 199614-92-1 199614-94-3
199614-95-4 199614-96-5 199614-97-6 199614-98-7 199614-99-8
199615-00-4 199615-01-5 199615-02-6 199615-03-7 199615-04-8
199615-05-9 199615-06-0 199615-08-2 199615-09-3 199615-10-6
199615-11-7 199615-12-8 199615-13-9 199615-14-0 199615-15-1
199615-16-2 199615-17-3 199615-18-4 199615-19-5 199615-20-8
199615-21-9 199615-22-0 199615-23-1 199615-24-2 199615-25-3
199615-26-4 199615-27-5 199615-28-6 199615-29-7 199615-34-4
199734-44-6 199734-45-7 199734-46-8

(cloning and cDNA sequences of mammalian calcium receptors and their
use in screening for compds. with potential action in the therapy of
disorders of calcium metabolism)

IT 7440-70-2, Calcium, biological studies

(cloning and cDNA sequences of mammalian calcium receptors and their
use in screening for compds. with potential action in the therapy of
disorders of calcium metabolism)

IT 153834-07-2 161048-76-6, Genbank U10354 163874-32-6, Genbank U20759
163874-33-7, Genbank U20760

(nucleotide sequence; cloning and cDNA sequences of mammalian calcium
receptors and their use in screening for compds. with potential action
in the therapy of disorders of calcium metabolism)

IT 9002-64-6, Parathormone 9007-12-9, Calcitonin

(secretion; cloning and cDNA sequences of mammalian calcium receptors
and their use in screening for compds. with potential action in the
therapy of disorders of calcium metabolism)

IT 586-37-8, 3'-Methoxyacetophenone 2038-57-5, 3-Phenylpropylamine

(synthesis and enantiomer resolution of NPS 467; cloning and cDNA
sequences of mammalian calcium receptors and their use in screening for
compds. with potential action in the therapy of disorders of calcium
metabolism)

IT 18655-48-6

(synthesis and enantiomer resolution of NPS R-568; cloning and cDNA
sequences of mammalian calcium receptors and their use in screening for
compds. with potential action in the therapy of disorders of calcium
metabolism)

IT 148717-47-9P, NPS 467

(synthesis and enantiomer resolution; cloning and cDNA sequences of
mammalian calcium receptors and their use in screening for compds. with
potential action in the therapy of disorders of calcium metabolism)

L8 ANSWER 20 OF 22 USPATFULL on STN

ACCESSION NUMBER: 97:107219 USPATFULL

TITLE: Calcium receptor-active molecules

INVENTOR(S): Brown, Edward M., Milton, MA, United States

Fuller, Forrest H., Salt Lake City, UT, United States
Hebert, Steven C., Wellesley, MA, United States
Garrett, Jr., James E., Salt Lake City, UT, United States

PATENT ASSIGNEE(S): The Brigham & Women's Hospital, Inc., Boston, MA,
United States (U.S. corporation)
NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 5688938 | | 19971118 |
| APPLICATION INFO.: | US 1995-485588 | | 19950607 (8) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1994-353784, filed on 8 Dec 1994 which is a continuation-in-part of Ser. No. US 1993-9389, filed on 23 Feb 1993, now abandoned Ser. No. Ser. No. US 1993-141248, filed on 22 Oct 1993, now abandoned And Ser. No. US 1994-292827, filed on 19 Aug 1994, now abandoned which is a continuation-in-part of Ser. No. US -141248 which is a continuation-in-part of Ser. No. US -9389 which is a continuation-in-part of Ser. No. US 1993-17127, filed on 12 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-934161, filed on 21 Aug 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-834044, filed on 11 Feb 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-749451, filed on 23 Aug 1991, now abandoned | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Walsh, Stephen | | |
| ASSISTANT EXAMINER: | Sorensen, Kenneth A. | | |
| LEGAL REPRESENTATIVE: | Lyons & Lyons LLP | | |
| NUMBER OF CLAIMS: | 24 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 111 Drawing Figure(s); 84 Drawing Page(s) | | |
| LINE COUNT: | 6522 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the different roles inorganic ion receptors have in cellular and body processes. The present invention features: (1) molecules which can modulate one or more inorganic ion receptor activities, preferably the molecule can mimic or block an effect of an extracellular ion on a cell having an inorganic ion receptor, more preferably the extracellular ion is Ca^{sup.2+} and the effect is on a cell having a calcium receptor; (2) inorganic ion receptor proteins and fragments thereof, preferably calcium receptor proteins and fragments thereof; (3) nucleic acids encoding inorganic ion receptor proteins and fragments thereof, preferably calcium receptor proteins and fragments thereof; (4) antibodies and fragments thereof, targeted to inorganic ion receptor proteins, preferably calcium receptor protein; and (5) uses of such molecules, proteins, nucleic acids and antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Thyroid gland
(C cell; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Antibiotics
(aminoglycoside; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Amines, biological studies
(aralkyl; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Ion channel blockers
(calcium; cloning and cDNA sequences of mammalian calcium receptors and

their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Receptors
(calcium; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Drug screening

IT Hyperparathyroidism

IT Molecular cloning

IT Osteoclast

IT Osteoporosis

IT Parathyroid gland

IT *Xenopus laevis*
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Antibodies
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Protamines
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT cDNA sequences
(for calcium receptors from cattle and human and rat)

IT Protein sequences
(of calcium receptors from cattle and human and rat)

IT Secretion (process)
(of parathormone or calcitonin; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Egg
(oocyte, *Xenopus*; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT Amines, biological studies
(polyamines, nonpolymeric; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 153834-08-3 161663-06-5 168183-63-9 168257-64-5
(amino acid sequence; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 159150-19-3P 179381-75-0P
(chemical syntheses of agonists/antagonists; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 93-08-3, 2'-Acetonaphthone 99-03-6, 3'-Aminoacetophenone 100-06-1, 4'-Methoxyacetophenone 122-03-2, 4-Isopropylbenzaldehyde 876-02-8, 4'-Hydroxy-3'-methylacetophenone 941-98-0, 1'-Acetonaphthone 1441-99-2, 3'-Thiomethylacetophenone 1504-74-1, 2-Methoxycinnamaldehyde 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 3886-70-2, (R)-(+)-1-(1-Naphthyl)ethylamine 4903-09-7 7315-17-5, 2-Chlorohydrocinnamionitrile 37612-52-5, 3'-Chloro-4'-methoxyacetophenone 68376-32-9, 2-Methylcinnamionitrile 88196-70-7
(chemical synthesis of agonists/antagonists; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 10024-90-5P 124829-13-6P
(chemical synthesis of agonists/antagonists; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 148717-54-8P, NPS R-568 179381-60-3P 179381-62-5P 179381-64-7P 179381-67-0P 179381-69-2P 199614-84-1P 199614-89-6P 199614-93-2P 199615-07-1P
(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 52-53-9, Verapamil 57-92-1, Streptomycin, biological studies 71-44-3, Spermine 112-24-3 112-57-2, Tetraethylenepentamine 119-04-0, Neomycin B 124-20-9, Spermidine 296-35-5, Hexacyclen 1403-66-3, Gentamicin 2783-17-7, 1,12-Dodecanediamine 4067-16-7, Pentaethylenehexamine 4696-76-8, Bekanamycin 7439-95-4, Magnesium, biological studies 13042-18-7, Fendiline 15834-81-8 16662-47-8, D-600 24937-47-1, Polyarginine 25104-18-1, Polylysine 25212-18-4, Polyarginine 33542-87-9 38000-06-5, Polylysine 38235-77-7 38235-77-7D, substituted derivs. 42399-41-7, Diltiazem 57818-92-5, TMB-8 66469-40-7 66469-40-7D, substituted derivs. 85610-72-6 87955-89-3, NPS 383 95956-62-0 105029-41-2, Argiotoxin-636 108393-62-0 108448-58-4, (-)-Fendiline 111944-83-3, Argiotoxin-659 128549-96-2, NPS 017 128549-97-3, NPS 015 133805-32-0, NPS 019 148717-48-0 148717-51-5 148717-52-6, NPS 384 148717-53-7 148717-56-0, NPS R-467 148740-50-5, NPS 381 148740-51-6, NPS 021 148740-52-7, NPS S-467 159149-49-2 159149-51-6 159149-75-4, NPS S-568 159149-76-5 159149-93-6 159149-96-9 159149-97-0 159150-00-2 **159150-01-3** 159150-03-5 159150-04-6 159150-06-8 159150-17-1 159150-29-5 159150-30-8 179381-56-7 179381-70-5 179381-74-9 179603-34-0 179603-37-3 179603-38-4 179603-41-9 179603-42-0 199614-29-4D, substituted derivs. 199614-33-0 199614-43-2 199614-44-3 199614-46-5 199614-48-7 199614-50-1 199614-53-4 199614-55-6 199614-57-8 199614-61-4 199614-63-6 199614-68-1 199614-73-8 199614-76-1 199614-77-2 199614-78-3 199614-79-4 199614-80-7 199614-81-8 199614-82-9 199614-83-0 199614-85-2 199614-86-3 199614-87-4 199614-88-5 199614-90-9 199614-91-0 199614-92-1 199614-94-3 199614-95-4 199614-96-5 199614-97-6 199614-98-7 199614-99-8 199615-00-4 199615-01-5 199615-02-6 199615-03-7 199615-04-8 199615-05-9 199615-06-0 199615-08-2 199615-09-3 199615-10-6 199615-11-7 199615-12-8 199615-13-9 199615-14-0 199615-15-1 199615-16-2 199615-17-3 199615-18-4 199615-19-5 199615-20-8 199615-21-9 199615-22-0 199615-23-1 199615-24-2 199615-25-3 199615-26-4 199615-27-5 199615-28-6 199615-29-7 199615-34-4 199734-44-6 199734-45-7 199734-46-8

(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 7440-70-2, Calcium, biological studies

(cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 153834-07-2 161048-76-6, Genbank U10354 163874-32-6, Genbank U20759 163874-33-7, Genbank U20760

(nucleotide sequence; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 9002-64-6, Parathormone 9007-12-9, Calcitonin

(secretion; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 586-37-8, 3'-Methoxyacetophenone 2038-57-5, 3-Phenylpropylamine

(synthesis and enantiomer resolution of NPS 467; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 18655-48-6

(synthesis and enantiomer resolution of NPS R-568; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

IT 148717-47-9P, NPS 467

(synthesis and enantiomer resolution; cloning and cDNA sequences of mammalian calcium receptors and their use in screening for compds. with potential action in the therapy of disorders of calcium metabolism)

pharmaceutically acceptable salts; a method for their preparation and method for their use

INVENTOR(S): Johansson, Rolf, Huddinge, Sweden
 Haraldsson, Martin, Taby, Sweden
 Ringberg, Erik, Uppsala, Sweden
 Vagberg, Ian, Sollentuna, Sweden
 Beierlein, Katarina, Uppsala, Sweden
 Emond, Rikard, Saltsjobaden, Sweden
 Sjoberg, Birger, Sollentuna, Sweden

PATENT ASSIGNEE(S): Pharmacia AB, Stockholm, Sweden (non-U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------------------|
| PATENT INFORMATION: | US 6313132 | B1 | 20011106 |
| | WO 9843942 | | 19981008 |
| APPLICATION INFO.: | US 1999-381868 | | 19990927 (9) |
| | WO 1998-SE556 | | 19980326 |
| | | | 19990927 PCT 371 date |
| | | | 19990927 PCT 102(e) date |

DOCUMENT TYPE: Utility

FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Oswecki, Jane C.

LEGAL REPRESENTATIVE: Birch, Stewart, Kolasch & Birch, LLP

NUMBER OF CLAIMS: 33

EXEMPLARY CLAIM: 1

LINE COUNT: 2364

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel compounds of Formula (I) wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6, R.sup.7 and Ar are as defined in claim 1, their salts with physiologically acceptable acids and, when the compounds can be in the form of optical isomers, the racemic mixture and the individual enantiomers. The compounds have anticholinergic activity, and the invention also relates to the compounds of Formula (I), the use of the compounds of Formula (I) for preparing anticholinergic drugs, the use of the compounds of Formula (I) for treating urinary tract incontinence, and methods for preparing the compounds of Formula (I). ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Bladder
 (incontinence, treatment; preparation of arylphenylpropanamines as anticholinergic agents)

IT Cholinergic antagonists

IT Muscarinic antagonists
 (preparation of arylphenylpropanamines as anticholinergic agents)

IT 214602-04-7P
 (byproduct; preparation of arylphenylpropanamines as anticholinergic agents)

IT 3699-80-7P 31600-86-9P, 2-Methoxyphenyllithium 42287-97-8P,
 3-Cyano-3-phenylpropanoic acid 55030-30-3P 56265-39-5P 56951-42-9P
 124937-29-7P 214601-34-0P 214601-35-1P 214601-36-2P 214601-37-3P
 214601-38-4P 214601-39-5P 214601-40-8P 214601-41-9P 214601-42-0P
 214601-43-1P 214601-44-2P 214601-45-3P 214601-46-4P 214601-47-5P
 214601-48-6P 214601-49-7P 214601-50-0P 214601-51-1P 214601-52-2P
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 214601-64-6P 214601-66-8P 214601-67-9P 214601-68-0P 214601-70-4P
 214601-71-5P 214601-72-6P 214601-73-7P 214601-74-8P 214601-75-9P
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 214601-86-2P 214601-87-3P 214601-88-4P 214601-89-5P 214601-90-8P
 214601-91-9P 214601-92-0P
 (intermediate; preparation of arylphenylpropanamines as anticholinergic agents)

IT 214601-12-4P 214852-24-1P 214852-28-5P 214852-31-0P
 (preparation of arylphenylpropanamines as anticholinergic agents)

IT 214600-36-9P 214600-37-0P 214600-38-1P 214600-39-2P 214600-40-5P
 214600-41-6P 214600-42-7P 214600-44-9P 214600-45-0P 214600-46-1P
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 214600-52-9P 214600-53-0P 214600-54-1P 214600-55-2P 214600-56-3P

214600-57-4P 214600-58-5P **214600-59-6P** 214600-60-9P
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 214852-38-7P 214853-02-8P

(preparation of arylphenylpropanamines as anticholinergic agents)

IT 95-55-6, o-Aminophenol 96-79-7 98-01-1, Furfural, reactions
 100-54-9, 3-Cyanopyridine 100-60-7, N-Methylcyclohexylamine 102-97-6,
 N-Benzylisopropylamine 103-36-6, Ethyl cinnamate 106-49-0,
 p-Methylaniline, reactions 140-29-4, Benzyl cyanide 342-24-5,
 2-Fluorobenzophenone 498-62-4, Thiophene-3-aldehyde 576-26-1
 578-57-4, 2-Bromoanisole 593-75-9, Methyl isonitrile 623-46-1,
 1,2-Dichloroethyl ether 727-99-1, 2-(Trifluoromethyl)benzophenone
 867-13-0, Triethyl phosphonoacetate 929-06-6, 2-(2-Aminoethoxy)ethanol
 1003-03-8, Cyclopentylamine 1003-09-4, 2-Bromothiophene 1192-58-1
 2516-34-9, Cyclobutylamine 2835-77-0, 2-Aminobenzophenone 5452-35-7,
 Cycloheptylamine 16202-11-2 17814-85-6, (4-
 Carboxybutyl)triphenylphosphonium bromide 44975-46-4,
 N,N-Diisopropylacrylamide 51321-61-0 113368-99-3 156755-25-8
 156755-28-1 156755-31-6 156755-34-9 207679-81-0 214601-93-1
 214601-94-2 214601-97-5 214602-00-3
 (starting material; preparation of arylphenylpropanamines as anticholinergic
 agents)

L8 ANSWER 22 OF 22 USPATFULL on STN
 ACCESSION NUMBER: 2001:48117 USPATFULL
 TITLE: Calcium receptor-active compounds
 INVENTOR(S): Van Wagenen, Bradford C., Salt Lake City, UT, United
 States
 Moe, Scott T., Salt Lake City, UT, United States
 Balandrin, Manuel F., Sandy, UT, United States
 DelMar, Eric G., Salt Lake City, UT, United States
 Nemeth, Edward F., Salt Lake City, UT, United States
 PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United
 States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|--|------|--------------|
| PATENT INFORMATION: | US 6211244 | B1 | 20010403 |
| APPLICATION INFO.: | US 1995-546998 | | 19951023 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Geist, Gary | | |
| ASSISTANT EXAMINER: | Padmanabhan, Sreeni | | |
| NUMBER OF CLAIMS: | 46 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 137 Drawing Figure(s); 104 Drawing Page(s) | | |
| LINE COUNT: | 3074 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention features compounds able to modulate one or more
 activities of an inorganic ion receptor and methods for treating
 diseases or disorders by modulating inorganic ion receptor activity.
 Preferably, the compound can mimic or block the effect of extracellular
 Ca.sup.2+ on a calcium receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT Receptors
 (calcium, mediated disorders; treatment; preparation of 1-arylethylamines as
 calcium receptor ligands)

| | | | | | |
|----|---|--------------|---------------------|--------------|--------------|
| IT | Parathyroid gland (modulators; preparation of 1-arylethylamines as calcium receptor ligands) | | | | |
| IT | Bone (resorption, inhibitors; preparation of 1-arylethylamines as calcium receptor ligands) | | | | |
| IT | 179381-77-2P 179381-81-8P (preparation of 1-arylethylamines as calcium receptor ligands) | | | | |
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| | 332078-46-3P | 332078-47-4P | 332078-48-5P | 332078-50-9P | |
| | (preparation of 1-arylethylamines as calcium receptor ligands) | | | | |
| IT | 332078-51-0P | 332078-52-1P | 332078-53-2P | 332078-54-3P | 332078-55-4P |
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| | 332078-66-7P | 332078-67-8P | 332078-68-9P | 332078-69-0P | 332078-70-3P |
| | 332078-71-4P | 332078-72-5P | 332078-73-6P | 332078-74-7P | 332078-75-8P |
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| | 332078-81-6P | 332078-82-7P | 332078-83-8P | 332078-84-9P | 332078-85-0P |
| | 332078-86-1P | 332078-87-2P | 332078-88-3P | 332078-89-4P | 332078-90-7P |
| | 332078-91-8P | 332078-92-9P | 332078-93-0P | 332078-94-1P | 332078-95-2P |
| | 332078-96-3P | 332078-97-4P | 332078-98-5P | 332078-99-6P | 332079-00-2P |
| | 332079-01-3P | 332079-02-4P | 332079-03-5P | | |
| | (preparation of 1-arylethylamines as calcium receptor ligands) | | | | |
| IT | 89-98-5, o-Chlorobenzaldehyde 93-08-3 99-02-5 99-03-6 99-91-2 | | | | |
| | 100-06-1 104-88-1, 4-Chlorobenzaldehyde, reactions 122-03-2, | | | | |

4-Isopropylbenzaldehyde 454-89-7, 3-Trifluoromethylbenzaldehyde
 532-27-4, 2-Chloroacetophenone 587-04-2, 3-Chlorobenzaldehyde
 876-02-8 941-98-0, 1-Acetonaphthone 943-27-1 1197-33-7,
 α-Methylcinnamionitrile 1504-74-1, 2-Methoxycinnamaldehyde
 1896-62-4, trans-4-Phenyl-3-buten-2-one 2038-57-5, 3-Phenylpropylamine
 2420-16-8, 3-Chloro-4-hydroxybenzaldehyde 2550-26-7,
 4-Phenyl)-2-butanone 3886-69-9 3886-70-2, (R)-1-(1-
 Naphthyl)ethylamine 4360-47-8, Cinnamionitrile 5586-73-2,
 3,3-Diphenylpropylamine 7315-17-5, 2-Chlorohydrocinnamionitrile
 28446-70-0 28446-71-1, 3-Methylcinnamionitrile 29127-79-5
 52771-21-8, 3-Trifluoromethoxybenzaldehyde 62409-13-6,
 1-(3-Methoxyphenyl)ethylamine 67646-72-4, 4-(3-Trifluoromethylphenyl)-2-
 butanone 68376-32-9, 2-Methylcinnamionitrile 83016-29-9 88196-70-7,
 (R)-3-Methoxy-α-methylbenzylamine 157524-86-2 179381-96-5
 (preparation of 1-arylethylamines as calcium receptor ligands)
 IT 1441-99-2P, 1-(3-Methylthiophenyl)ethanone 4903-09-7P,
 3-Chloro-4-methoxybenzaldehyde 10024-90-5P, 1-(4-Methoxy-3-
 Methylphenyl)ethanone 18655-49-7P, 3-(3-Chlorophenyl)propylamine
 24654-47-5P 37612-52-5P, 3'-Chloro-4'-methoxyacetophenone
 124829-13-6P, 3-Chloro-4-methoxy-α-methylbenzenemethanol
 168833-77-0P 173252-77-2P 179381-92-1P 179381-93-2P 179381-94-3P,
 4-(3-Trifluoromethoxyphenyl)-2-butanone 179381-97-6P
 (preparation of 1-arylethylamines as calcium receptor ligands)
 IT 206370-65-2 206370-66-3
 (unclaimed nucleotide sequence; preparation of 1-arylethylamines as calcium
 receptor ligands)

=> FIL REGISTRY

| | | |
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| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 82.71 | 254.22 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -3.75 | -3.75 |

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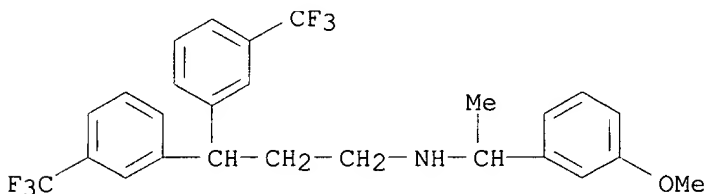
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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 159150-01-3 REGISTRY
CN Benzenepropanamine, N-[1-(3-methoxyphenyl)ethyl]-3-(trifluoromethyl)-
γ-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H25 F6 N O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA Caplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP
(Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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NOTICE SET TO OFF FOR DISPLAY COMMAND
SET COMMAND COMPLETED

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REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:74531 CAPLUS

DOCUMENT NUMBER: 132:342594

TITLE: NPS 1506, a novel NMDA receptor antagonist and neuroprotectant: Review of preclinical and clinical studies

AUTHOR(S): Mueller, Alan L.; Artman, Linda D.; Balandrin, Manuel F.; Brady, Ellen; Chien, Yongwei; Delmar, Eric G.; George, Karen; Kierstead, Allison; Marriott, Thomas B.; Moe, Scott T.; Newman, Michael K.; Raszkiewicz, Joanna L.; Sanguinetti, Elizabeth L.; Van Wagenen, Bradford C.; Wells, David

CORPORATE SOURCE: NPS Pharmaceuticals, Inc., Salt Lake City, UT, 84108, USA

SOURCE: Annals of the New York Academy of Sciences (1999), 890 (Neuroprotective Agents), 450-457
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

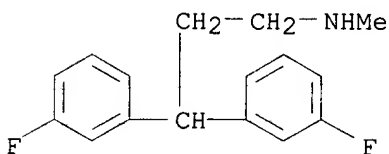
AB A review with 10 refs. NPS 1506 is a moderate-affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist. NPS 1506 is neuroprotective in rodent models of ischemic stroke, hemorrhagic stroke, and head trauma, with a 2-h window of opportunity. Neuroprotectant doses of NPS 1506 ranged approx. 0.1-1.0 mg/kg, with peak plasma concns. of 8-80 ng/mL. Even at doses producing behavioral toxicity, NPS 1506 did not elicit MK-801-like behaviors, did not generalize to phencyclidine (PCP), and did not elicit neuronal vacuolization. In a Phase I study, i.v. doses of NPS 1506 of 5-100 mg were well tolerated and provided plasma concns. in excess of those required for neuroprotection in rodents. Adverse events at the 100-mg dose included mild dizziness and lightheadedness, and mild to moderate ataxia. Neither PCP-like psychotomimetic effects nor cardiovascular effects were noted. The long plasma half-life of NPS 1506 (.apprx.60 h) suggests that a single i.v. dose will provide prolonged neuroprotection in humans.

IT 186495-99-8, NPS 1506

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists
(NMDA antagonists; NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

IT Cytoprotective agents
(neuroprotectants; NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

IT 186495-99-8, NPS 1506

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:66753 CAPLUS

DOCUMENT NUMBER: 132:107773

TITLE: Preparation of aralkylamines as NMDA receptor-ionophore complex antagonists

INVENTOR(S): Mueller, Alan L.; Balandrin, Manuel F.; Vanwagenen, Bradford C.; Moe, Scott T.; Delmar, Eric G.; Artman, Linda D.; Barmore, Robert M.; Smith, Daryl L.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: U.S., 112 pp., Cont.-in-part of U.S. Ser. No. 663.013. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| US 6017965 | A | 20000125 | US 1996-763480 | 19961211 |
| CA 2182680 | AA | 19950817 | CA 1994-2182680 | 19941026 |
| WO 9521612 | A2 | 19950817 | WO 1994-US12293 | 19941026 |
| WO 9521612 | A3 | 19950921 | | |
| W: | AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US | | | |
| RW: | KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| CN 1148337 | A | 19970423 | CN 1994-195074 | 19941026 |
| CN 1088585 | B | 20020807 | | |
| ES 2156162 | T3 | 20010616 | ES 1994-932057 | 19941026 |
| EP 1123922 | A2 | 20010816 | EP 2000-121960 | 19941026 |
| EP 1123922 | A3 | 20040102 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | |
| PT 743853 | T | 20011031 | PT 1994-932057 | 19941026 |
| US 6071970 | A | 20000606 | US 1995-485038 | 19950607 |
| CA 2257234 | AA | 19971211 | CA 1996-2257234 | 19961211 |
| US 6211245 | B1 | 20010403 | US 1998-186341 | 19981104 |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| US 2002004522 | A1 | 20020110 | US 2001-825373 | 20010402 |
| US 6750244 | B2 | 20040615 | | |
| JP 2004002437 | A2 | 20040108 | JP 2003-158350 | 20030603 |
| US 2004171670 | A1 | 20040902 | US 2004-797355 | 20040309 |
| PRIORITY APPLN. INFO.: | | | US 1993-14813 | B2 19930208 |
| | | | US 1994-194210 | B2 19940208 |
| | | | US 1994-288668 | B2 19940809 |
| | | | WO 1994-US12293 | A2 19941026 |
| | | | US 1995-485038 | A2 19950607 |
| | | | US 1996-663013 | A2 19960607 |
| | | | US 1994-288688 | A2 19940811 |
| | | | EP 1994-932057 | A3 19941026 |
| | | | JP 1995-521191 | A3 19941026 |
| | | | WO 1996-US19525 | A 19961206 |
| | | | AU 1997-13525 | A3 19961211 |
| | | | US 1996-763480 | A2 19961211 |
| | | | US 1997-869154 | B2 19970604 |
| | | | US 1997-873011 | A1 19970611 |
| | | | US 1998-186341 | A1 19981104 |
| | | | US 2001-825373 | A1 20010402 |

OTHER SOURCE(S): MARPAT 132:107773

AB R7CHR4CR1R5CRR2R6[I; R = H or N(R3)2; R1,R5 = (un)substituted Ph, -CH2Ph, -OPh; R2,R6 = H or (hydroxy)alkyl; R1R2 = (CH2)n or (CH2)nNR3(CH2)n; R2R6

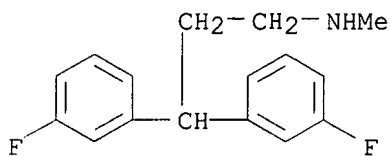
= NH; R3 = H, alkyl, CH₂CH₂OH, alkylphenyl; R4 = (un)substituted Ph, -pyridyl, -thienyl, etc.; R7 = (un)substituted Ph; n = 0-6] were prepared Thus, (3-FC₆H₄)₂CO was condensed with (EtO)₂P(O)CH₂CO₂Et and the product converted in 6 steps to (3-FC₆H₄)₂CHCH₂CHMeNH₂. Data for biol. activity of I were given.

IT 186495-49-8P 186495-55-6P 186495-56-7P
186495-99-8P 200429-55-6P 200429-70-5P
200429-72-7P 200430-06-4P 200430-16-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

RN 186495-49-8 CAPLUS

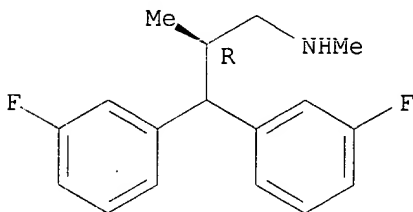
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 186495-55-6 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,β-dimethyl-, (βR)- (9CI) (CA INDEX NAME)

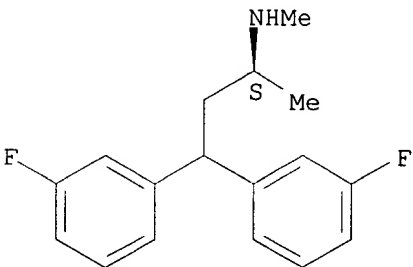
Absolute stereochemistry.



RN 186495-56-7 CAPLUS

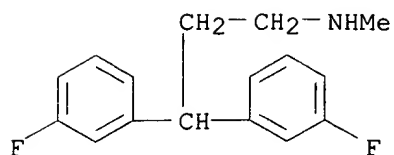
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,α-dimethyl-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186495-99-8 CAPLUS

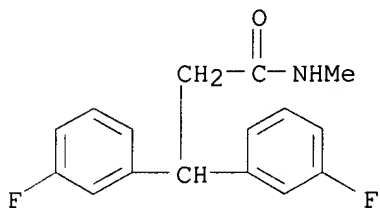
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

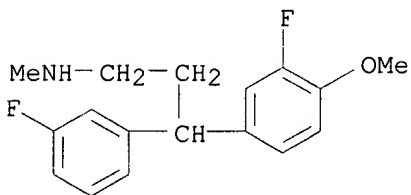
RN 200429-55-6 CAPLUS

CN Benzenepropanamide, 3-fluoro- β -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



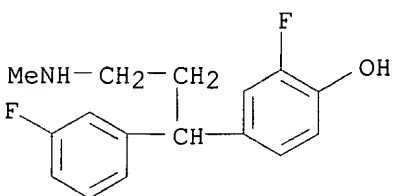
RN 200429-70-5 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-4-methoxy-N-methyl- (9CI) (CA INDEX NAME)



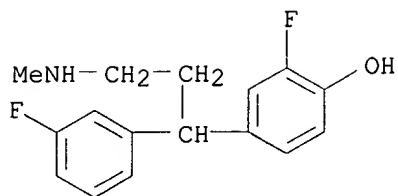
RN 200429-72-7 CAPLUS

CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]- (9CI) (CA INDEX NAME)



RN 200430-06-4 CAPLUS

CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]-, hydrochloride (9CI) (CA INDEX NAME)

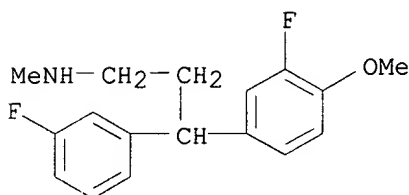


● HCl

RN 200430-16-6 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-,
 (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

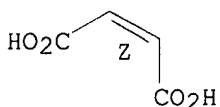
CRN 200429-70-5
 CMF C17 H19 F2 N O



CM 2

CRN 110-16-7
 CMF C4 H4 O4

Double bond geometry as shown.



IT Calcium channel
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (NMDA-binding glutamate receptor complex, antagonists; preparation of
 aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (NMDA-binding, calcium channel complexes, antagonists; preparation of
 aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Nervous system
 (disease, treatment; preparation of aralkylamines as NMDA receptor-ionophore
 complex antagonists)

IT Glutamate receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (methyl-D-aspartate-binding, calcium channel complexes, antagonists;
 preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Cytoprotective agents
 (neuroprotectants; preparation of aralkylamines as NMDA receptor-ionophore
 complex antagonists)

IT Analgesics

Anticonvulsants

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 5586-73-2P, 3,3-Diphenylpropylamine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
5666-18-2P 14451-09-3P, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
17349-94-9P 19841-73-7P 21745-77-7P, 9H-Xanthene-9-ethanamine
21745-81-3P, 9H-Thioxanthene-9-ethanamine 21745-82-4P 21745-83-5P
21745-85-7P 28075-29-8P 36765-74-9P 48166-95-6P 53179-07-0P
54910-89-3P 57226-64-9P 63940-51-2P 64630-52-0P 90531-05-8P
91472-94-5P 95956-62-0P 98383-47-2P 98383-56-3P 106359-50-6P
109306-10-7P 114754-01-7P 114754-02-8P 114754-03-9P 114754-04-0P
118468-16-9P 144451-90-1P 144451-98-9P 144452-04-0P 144452-11-9P
159149-65-2P 170018-54-9P 170018-55-0P 170018-56-1P 170018-57-2P
170018-63-0P 170018-66-3P 170018-67-4P 170018-68-5P 170018-71-0P
170018-72-1P 170018-73-2P 170018-74-3P 170018-75-4P 170018-76-5P
170018-77-6P 170018-78-7P 170018-79-8P 170018-80-1P 170018-81-2P
170018-82-3P 170018-83-4P 170018-84-5P 170018-85-6P 170018-86-7P
170019-10-0P 186495-37-4P 186495-38-5P 186495-39-6P 186495-40-9P
186495-41-0P 186495-42-1P 186495-43-2P 186495-44-3P 186495-45-4P
186495-46-5P 186495-47-6P 186495-48-7P **186495-49-8P**
186495-50-1P 186495-51-2P 186495-52-3P 186495-53-4P 186495-54-5P
186495-55-6P **186495-56-7P** 186495-57-8P 186495-58-9P
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186495-69-2P 186495-70-5P 186495-71-6P 186495-72-7P 186495-73-8P
186495-74-9P 186495-75-0P 186495-76-1P 186495-77-2P 186495-78-3P
186495-79-4P 186495-80-7P 186495-81-8P 186495-82-9P 186495-84-1P
186495-86-3P 186495-87-4P 186495-88-5P 186495-89-6P 186495-90-9P
186495-91-0P 186495-92-1P 186495-93-2P 186495-94-3P 186495-95-4P
186495-97-6P 186495-98-7P **186495-99-8P** 186496-00-4P
186496-01-5P 186496-02-6P 186496-03-7P 186496-04-8P 186496-05-9P
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186496-11-7P 186496-12-8P 186496-13-9P 186496-14-0P 186496-15-1P
186496-16-2P 186496-17-3P 186496-20-8P 186496-21-9P 186496-22-0P
186496-23-1P 186496-24-2P 186496-25-3P 186496-26-4P 186496-27-5P
186496-29-7P 186496-30-0P 186496-71-9P 200420-69-5P 200427-53-8P
200429-46-5P 200429-48-7P 200429-49-8P 200429-50-1P 200429-51-2P
200429-52-3P 200429-53-4P 200429-54-5P **200429-55-6P**
200429-56-7P 200429-57-8P 200429-58-9P 200429-59-0P 200429-60-3P
200429-61-4P 200429-62-5P 200429-63-6P 200429-64-7P 200429-65-8P
200429-67-0P 200429-68-1P 200429-69-2P **200429-70-5P**
200429-71-6P **200429-72-7P** 200429-73-8P 200429-74-9P
200429-75-0P 200429-79-4P 200429-80-7P 200429-86-3P 200429-87-4P
200430-04-2P 200430-05-3P **200430-06-4P** 200430-07-5P
200430-08-6P 200430-14-4P **200430-16-6P** 200430-18-8P
200430-19-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 85-41-6, Phthalimide 103-67-3, N-Methylbenzylamine 135-02-4,
o-Anisaldehyde 140-88-5 285-67-6, Cyclopentene oxide 345-70-0,
3,3'-Difluorobenzophenone 351-54-2, 3-Fluoro-p-anisaldehyde 372-20-3,
3-Fluorophenol 452-08-4, 2-Bromo-4-fluoroanisole 456-48-4,
3-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 578-57-4,
2-Bromoanisole 587-04-2, 3-Chlorobenzaldehyde 610-99-1 932-31-0,
2-Methylphenylmagnesium bromide 1073-06-9, 1-Bromo-3-fluorobenzene
1210-35-1, Dibenzosuberone 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one
17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2,
(S)-N-Benzyl- α -methylbenzylamine 18707-60-3, Methyl crotonate
20595-30-6, Trans-3-Fluorocinnamic acid 21900-39-0, 5-Fluoro-2-

methylbenzoyl chloride 65416-24-2, Benzyl crotonate 77532-79-7,
5-Fluoro-2-methylbenzonitrile 100306-34-1 147624-13-3,
3-Fluoro-2-methylbenzaldehyde 170019-09-7, 3,3-Bis(3-
fluorophenyl)propionitrile 186496-59-3, 5-Fluoro-2-methylphenylmagnesium
bromide

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

IT 455-67-4P 458-45-7P 701-38-2P 5561-92-2P, 1-(2-Methoxyphenyl)-1-
propanone 15966-37-7P 21745-42-6P 21745-68-6P 25772-94-5P
38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P
156868-83-6P, 3-(3-Fluorophenyl)-1-propanol 170019-11-1P 170019-14-4P,
Ethyl 3,3-bis(3-fluorophenyl)propionate 170019-15-5P 170019-16-6P
170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P 170019-21-3P
170019-22-4P 170019-23-5P 170019-24-6P 170019-25-7P 186496-34-4P
186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P
186496-40-2P 186496-41-3P 186496-42-4P 186496-44-6P 186496-45-7P
186496-46-8P 186496-48-0P 186496-49-1P 186496-50-4P 186496-51-5P
186496-52-6P 186496-53-7P 186496-57-1P 186496-58-2P 186496-60-6P
200430-09-7P 200430-10-0P 200430-11-1P 200430-12-2P,
3,3'-Difluoro-4-methoxybenzophenone 200430-13-3P 200430-15-5P
200430-17-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

REFERENCE COUNT: 172 THERE ARE 172 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:53380 CAPLUS

DOCUMENT NUMBER: 132:93096

TITLE: Preparation of diarylalkylamines and related compounds
active at both the serotonin reuptake site and the
N-methyl-D-aspartate receptor for treatment depression
and other disorders.

INVENTOR(S): Mueller, Alan; Moe, Scott; Balandrin, Manuel

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2000002551 | A2 | 20000120 | WO 1999-US15857 | 19990712 |
| WO 2000002551 | A3 | 20000921 | | |
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| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2336962 | AA | 20000120 | CA 1999-2336962 | 19990712 |
| AU 9949919 | A1 | 20000201 | AU 1999-49919 | 19990712 |
| AU 771252 | B2 | 20040318 | | |
| EP 1096926 | A2 | 20010509 | EP 1999-933987 | 19990712 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| US 2004039014 | A1 | 20040226 | US 2001-990405 | 20011121 |
| PRIORITY APPLN. INFO.: | | | US 1998-92546P | P 19980713 |
| | | | WO 1999-US15857 | W 19990712 |

OTHER SOURCE(S): MARPAT 132:93096

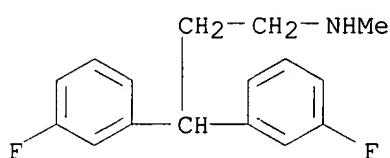
AB A method for treatment of depression comprises administration of a compound having NMDA receptor binding activity of $IC_{50} = 50 \text{ nM}$ to $1 \mu\text{M}$ and serotonin reuptake $IC_{50} \leq 100 \text{ nM}$. The compds. include e.g. $XmAr1(XmAr2)CHCR1R1CR2R2NR3R3$ [$X = \text{Br, Cl, F, iodo, CF}_3, \text{alkyl, OH, OCF}_3, \text{alkoxy, acyloxy; Ar1, Ar2} = \text{Ph, naphthyl, thiofuranyl, tetrahydronaphthyl, furyl, pyridyl, etc.; R1} = \text{H, alkyl, hydroxyalkyl, OH, alkoxy, acyloxy; R2} = \text{H, alkyl, hydroxyalkyl; (R2)}_2 = \text{imino; R3} = \text{H, alkyl, HOCH}_2\text{CH}_2, \text{alkylphenyl; m} = 0-5]$. Thus, N-methyl-bis-[3-(3-fluorophenyl)]propylamine (preparation given) at 5 mg/kg orally in mice produced a time-dependent reduction in the duration of immobility in the forced swimming test.

IT **186495-99-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists

(NMDA antagonists; preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT Antidepressants

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 5-HT receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(reuptake inhibitors; preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 21745-82-4P 21745-83-5P 50366-32-0P 186495-87-4P

186495-99-8P 186496-01-5P 200429-75-0P 200430-07-5P
255039-63-5P 255039-64-6P 255039-65-7P 255039-66-8P 255039-67-9P
255039-68-0P 255039-69-1P 255039-70-4P 255039-71-5P 255039-72-6P
255039-73-7P 255039-74-8P 255039-75-9P 255039-76-0P 255039-77-1P
255039-78-2P 255039-79-3P 255039-80-6P 255039-81-7P 255039-82-8P
255040-00-7P 255040-01-8P 255040-02-9P 255040-03-0P 255040-04-1P
255040-05-2P 255040-07-4P 255040-08-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 74-89-5, Methylamine, reactions 95-48-7, reactions 103-67-3,
N-Benzylmethylamine 140-88-5 345-69-7, 3-Fluorobenzophenone
345-70-0, 3,3'-Difluorobenzophenone 372-20-3, 3-Fluorophenol 395-23-3,
4-Trifluoromethylbenzhydrol 402-45-9, p-Trifluoromethylphenol
457-68-1, 4,4'-Difluorodiphenylmethane 529-20-4, o-Tolualdehyde
540-51-2, 2-Bromoethanol 590-17-0, Bromoacetonitrile 625-36-5,
3-Chloropropionyl chloride 932-31-0, o-Tolylmagnesium bromide

933-88-0, o-Toluoyl chloride 1073-06-9, 3-Bromofluorobenzene
1210-35-1, Dibenzosuberone 2537-48-6, Diethyl cyanomethylphosphonate
20595-30-6, trans-3-Fluorocinnamic acid 72551-53-2 100306-33-0
100306-34-1 186496-23-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 365-17-3P 458-45-7P 1018-97-9P 15966-37-7P 25772-94-5P
38158-75-7P 50499-52-0P 53915-75-6P 69096-48-6P 83406-26-2P
84648-43-1P 98586-21-1P 156868-83-6P 186496-49-1P 186496-50-4P
186496-57-1P 186496-58-2P 186496-60-6P 200430-09-7P 200430-10-0P
200430-17-7P 255039-83-9P 255039-84-0P 255039-85-1P 255039-86-2P
255039-87-3P 255039-88-4P 255039-89-5P 255039-90-8P 255039-91-9P
255039-92-0P 255039-93-1P 255039-94-2P 255039-95-3P 255039-96-4P
255039-97-5P 255039-98-6P 255039-99-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

L3 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:388157 CAPLUS

DOCUMENT NUMBER: 131:44658

TITLE: Preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents.

INVENTOR(S): Balandrin, Manuel F.; Vanwagenen, Bradford C.; Artman, Linda D.; Mueller, Alan L.; Smith, Daryl

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

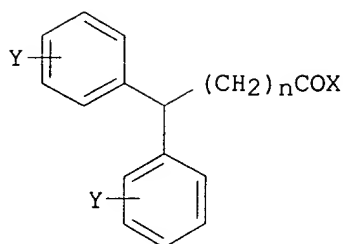
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9929657 | A1 | 19990617 | WO 1998-US26315 | 19981209 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2313236 | AA | 19990617 | CA 1998-2313236 | 19981209 |
| AU 9918170 | A1 | 19990628 | AU 1999-18170 | 19981209 |
| AU 763245 | B2 | 20030717 | | |
| EP 1042275 | A1 | 20001011 | EP 1998-963065 | 19981209 |
| EP 1042275 | B1 | 20051109 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001525390 | T2 | 20011211 | JP 2000-524254 | 19981209 |
| NZ 524395 | A | 20041029 | NZ 1998-524395 | 19981209 |
| IL 136306 | A1 | 20050925 | IL 1998-136306 | 19981209 |
| AT 309200 | E | 20051115 | AT 1998-963065 | 19981209 |
| US 6617358 | B1 | 20030909 | US 2000-587179 | 20000602 |
| US 2003199589 | A1 | 20031023 | US 2003-429060 | 20030502 |
| PRIORITY APPLN. INFO.: | | | US 1997-69005P | P 19971210 |
| | | | WO 1998-US26315 | W 19981209 |
| | | | US 2000-587179 | A1 20000602 |

OTHER SOURCE(S): MARPAT 131:44658

GI

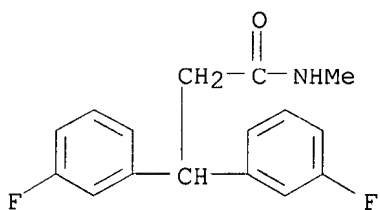


AB Title compds. (I; Y = H, F, Cl; X = NR₁R₂, OR₁; R₁ = H, alkyl, hydroxyalkyl; R₂ = H, Me, Et; n = 0-4; with specific exceptions), were prepared for treatment of seizure disorder, neurodegenerative disease, anxiety, stress, multiple sclerosis, Parkinson's disease, migraine, etc. (no data). Thus, 4,4-bis(4-fluorophenyl)butyl chloride was treated successively with KOAc in DMF, NaOH in EtOH/H₂O, CrO₃/H₂SO₄ in H₂O/acetone, SOCl₂, and NH₃ in H₂O/EtOAc to give 4,4-bis(4-fluorophenyl)butanamide.

IT **200429-55-6P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

RN 200429-55-6 CAPLUS

CN Benzenepropanamide, 3-fluoro-β-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT Nervous system
 (Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system
 (amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Spinal cord
 (injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (manic bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (mood-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Anti-Alzheimer's agents
 Anticonvulsants
 Antimigraine agents
 Antiparkinsonian agents
 Anxiolytics
 Nervous system agents
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Brain, disease
 (stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Head
(trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Multiple sclerosis
(treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P 200429-53-4P
200429-54-5P **200429-55-6P** 227289-95-4P 227290-02-0P
227290-09-7P 227290-12-2P 227290-22-4P 227290-28-0P 227290-37-1P
227290-41-7P 227290-47-3P 227290-50-8P 227290-56-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions
124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,
4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,
Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,
Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate
3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P
50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P
170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P
227290-64-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:7958 CAPLUS

DOCUMENT NUMBER: 130:66268

TITLE: Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

INVENTOR(S): Mueller, Alan L.; Moe, Scott T.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 252 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|-----------|-----------------|-------------|
| WO 9856752 | A1 | 19981217 | WO 1998-US11608 | 19980611 |
| W: JP | | | | |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| PRIORITY APPLN. INFO.: | | | US 1997-873011 | A 19970611 |
| | | | AU 1997-13525 | A3 19961211 |
| OTHER SOURCE(S): | MARPAT | 130:66268 | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The compds. [I, II, III; R1 and R3 are independently selected from (un)substituted Ph, benzyl, phenoxy, H, alkyl, OH, etc.; R2 and R5 are independently selected from H, alkyl, hydroxyalkyl; R2-R5 together are

imino; R1-R2 together are (CH2)n, (CH2)n-N(R6)-(CH2)n; n = 0-6, at least one n greater than 0; R6 is H, alkyl, 2-hydroxyethyl, and alkylphenyl; R4 is selected from (un)substituted thiofuryl, pyridyl, Ph, benzyl, phenoxy, phenylthio, H, alkyl, chcloalkyl; X, X1 is independently selected from (un)substituted Ph, benzyl, phenoxy, F, Cl, Br, Oh, etc.; m = 0-5; Y is N(R6)2, H when R1-R2 together are (CH2)n-N(R6)-(CH2)n], pharmaceutical compns., and pharmaceutical acceptable salts, complexes, and carriers are prepared as antagonists of NMDA receptor-mediated responses for treating a neurol. disease or disorder such as stroke, head trauma, spinal cord injury, spinal cord ischemia, ischemia- or hypoxia-induced nerve cell damage, epilepsy, anxiety, neuropsychiatric or cognitive deficits due to ischemia or hypoxia such as those that frequently occur as a consequence of cardiac surgery under cardiopulmonary bypass, or neurodegenerative diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's Disease, or amyotrophic lateral sclerosis (ALS).

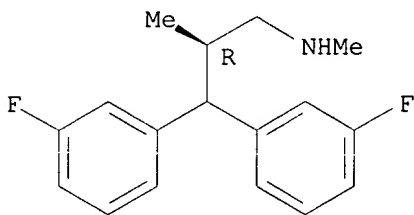
IT 186495-55-6P 186495-56-7P 186495-99-8P
200429-55-6P 200430-06-4P 200430-16-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

RN 186495-55-6 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,β-dimethyl-,
(βR)- (9CI) (CA INDEX NAME)

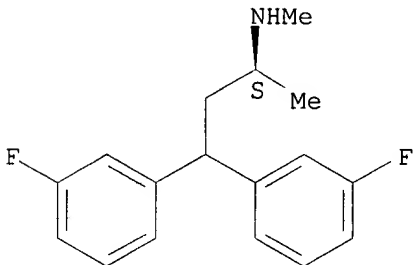
Absolute stereochemistry.



RN 186495-56-7 CAPLUS

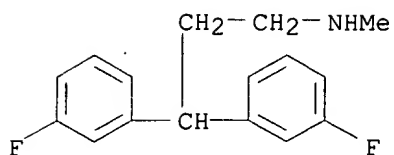
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,α-dimethyl-,
(αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



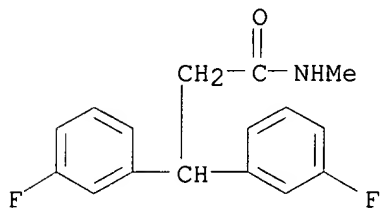
RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)

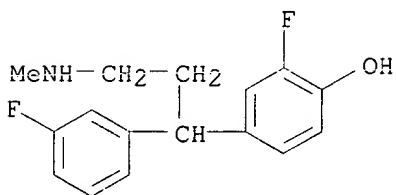


● HCl

RN 200429-55-6 CAPLUS
CN Benzenepropanamide, 3-fluoro-β-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 200430-06-4 CAPLUS
CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]-, hydrochloride (9CI) (CA INDEX NAME)

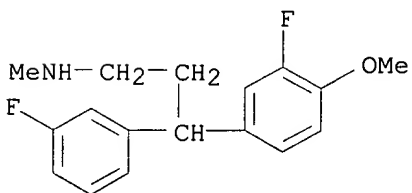


● HCl

RN 200430-16-6 CAPLUS
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

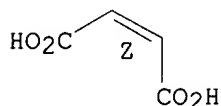
CRN 200429-70-5
CMF C17 H19 F2 N O



CM 2

CRN 110-16-7

Double bond geometry as shown.



IT Glutamate receptors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NMDA-binding; compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT Amines, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(aralkyl; compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT Asymmetric synthesis and induction

Drug delivery systems
(compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT Nervous system

(disease; compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 5586-73-2P 170018-57-2P 186495-38-5P 200430-19-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
5666-18-2P 14451-09-3P, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
17349-94-9P 19841-73-7P 21745-77-7P, 9H-Xanthene-9-ethanamine
21745-81-3P, 9H-Thioxanthene-9-ethanamine 21745-82-4P 28075-29-8P
36765-74-9P 48166-95-6P 53179-07-0P 54910-89-3P 57226-64-9P
63940-51-2P 64630-52-0P 90531-05-8P 91472-94-5P 95956-62-0P
98383-47-2P 98383-56-3P 106359-50-6P 109306-10-7P 114754-01-7P
114754-02-8P 114754-03-9P 114754-04-0P 116541-62-9P 118468-16-9P
144451-90-1P 144452-11-9P 159149-65-2P 170018-39-0P 170018-44-7P
170018-46-9P 170018-47-0P 170018-48-1P 170018-49-2P 170018-50-5P
170018-51-6P 170018-52-7P 170018-55-0P 170018-56-1P 170018-63-0P
170018-68-5P 170018-71-0P 170018-72-1P 170018-73-2P 170018-74-3P
170018-75-4P 170018-76-5P 170018-77-6P 170018-78-7P 170018-79-8P
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186495-89-6P 186495-90-9P 186495-91-0P 186495-93-2P 186495-94-3P
186495-95-4P 186495-97-6P **186495-99-8P** 186496-00-4P
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186496-07-1P 186496-09-3P 186496-10-6P 186496-11-7P 186496-12-8P
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186496-26-4P 186496-27-5P 186496-29-7P 186496-30-0P 186496-71-9P
200420-69-5P 200427-53-8P 200429-49-8P 200429-50-1P 200429-51-2P
200429-52-3P 200429-53-4P 200429-54-5P **200429-55-6P**

200429-56-7P 200429-57-8P 200429-58-9P 200429-59-0P 200429-60-3P
 200429-61-4P 200429-62-5P 200429-63-6P 200429-64-7P 200429-65-8P
 200429-67-0P 200429-69-2P 200429-73-8P 200429-74-9P 200429-75-0P
 200429-76-1P 200429-77-2P 200429-81-8P 200429-82-9P 200429-84-1P
 200430-05-3P **200430-06-4P** 200430-08-6P **200430-16-6P**
 200430-18-8P 217658-85-0P 217658-89-4P 217658-94-1P 217658-96-3P
 217659-01-3P 217659-23-9P 217659-76-2P 217660-61-2P 217660-91-8P
 217660-94-1P 217661-05-7P 217661-16-0P 217661-17-1P 217661-22-8P
 217661-23-9P 217661-24-0P 217661-26-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 50-47-5, Desipramine 50-48-6 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 58-73-1 59-32-5, Chlorpyramine 72-69-5, Nortriptyline 82-92-8, Cyclizine 82-93-9, Chlorcyclizine 86-21-5 86-22-6 113-92-8 144-11-6, Trihexyphenidyl 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 390-64-7, Prenylamine 438-60-8, Protriptyline 511-45-5, Pridinol 562-10-7 841-77-0, Nor-cyclizine 1668-19-5, Doxepin 2062-78-4, Pimozide 2095-87-6 3416-26-0, Lidoflazine 3737-09-5, Disopyramide 3963-62-0 7492-32-2, Isopropamide 10262-69-8, Maprotiline 56775-88-3, Zimeldine 108393-62-0 108448-58-4 133805-32-0 142275-74-9 144576-90-9 148920-48-3 217661-25-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 170018-54-9P 170019-10-0P
 RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 95-46-5, 2-Bromotoluene 100-39-0 103-67-3 105-34-0 135-02-4 140-88-5 285-67-6, Cyclopentene oxide 345-70-0 351-54-2 456-48-4 529-20-4 587-04-2 610-99-1 925-90-6, Ethyl magnesium bromide 1073-06-9 1210-35-1 2537-48-6, Diethyl cyanomethylphosphonate 2627-86-3 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one 17318-03-5, 3-Fluorophenyl magnesium bromide 20595-30-6 21900-39-0 22115-41-9 65416-24-2 77532-79-7 100306-33-0 147624-13-3 170019-09-7 186496-59-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 458-45-7P 1018-97-9P 1799-19-5P 1799-29-7P 2845-91-2P 5561-92-2P 15966-37-7P 17480-69-2P 21745-42-6P 21745-68-6P 25772-94-5P 32019-30-0P 34841-35-5P 38158-77-9P 75762-57-1P 84648-43-1P 93559-81-0P 98586-06-2P 98586-21-1P 125025-34-5P 156868-83-6P 170019-11-1P 170019-12-2P 170019-13-3P 170019-14-4P 170019-15-5P 170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P, Ethyl 3,3-bis(3-fluorophenyl)acrylate 170019-23-5P, 3,3-Bis(3-fluorophenyl)propionic acid 170019-24-6P, 4,4-Bis(3-fluorophenyl)-2-butanone 170019-25-7P 186496-31-1P 186496-32-2P 186496-33-3P 186496-34-4P 186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P 186496-40-2P 186496-41-3P 186496-42-4P 186496-43-5P 186496-44-6P 186496-45-7P 186496-46-8P 186496-47-9P 186496-48-0P 186496-49-1P 186496-50-4P 186496-54-8P 186496-55-9P 186496-56-0P 186496-57-1P 186496-58-2P 186496-60-6P 200430-11-1P 200430-12-2P 200430-13-3P 200430-14-4P 200430-17-7P 217661-27-3P 217661-28-4P 217661-29-5P 217661-30-8P 217661-31-9P 217661-32-0P 217661-33-1P 217661-34-2P 217661-35-3P 217661-40-0P 217661-42-2P 217661-44-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:1444 CAPLUS

DOCUMENT NUMBER: 128:61341

TITLE: Preparation of aralkylamines as NMDA receptor-ionophore complex antagonists

INVENTOR(S): Mueller, Alan L.; Moe, Scott T.; Balandrin, Manuel F.; Vanwagenen, Bradford C.; Delmar, Eric G.; Artman, Linda D.; Barmore, Robert M.; Smith, Daryl L.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 298 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9746511 | A1 | 19971211 | WO 1996-US20697 | 19961211 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2257234 | AA | 19971211 | CA 1996-2257234 | 19961211 |
| AU 9713525 | A1 | 19980105 | AU 1997-13525 | 19961211 |
| AU 723349 | B2 | 20000824 | | |
| EP 912494 | A1 | 19990506 | EP 1996-945069 | 19961211 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002511835 | T2 | 20020416 | JP 1998-500538 | 19961211 |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| PRIORITY APPLN. INFO.: | | | US 1996-663013 | A 19960607 |
| | | | WO 1996-US19525 | A 19961206 |
| | | | AU 1997-13525 | A3 19961211 |
| | | | WO 1996-US20697 | W 19961211 |

OTHER SOURCE(S): MARPAT 128:61341

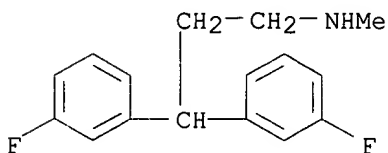
AB R7CHR4CR1R5CRR2R6 [I; R = H or N(R3)2; R1,R5 = (un)substituted Ph, -CH2Ph, -OPh; R2,R6 = H or (hydroxy)alkyl; R1R2 = (CH2)n or (CH2)nNR3(CH2)n; R2R6 = NH; R3 = H, alkyl, CH2CH2OH, alkylphenyl; R4 = (un)substituted Ph, -pyridyl, -thienyl, etc.; R7 = (un)substituted Ph; n = 0-6] were prepared Thus, (3-FC6H4)2CO was condensed with (EtO)2P(O)CH2CO2Et and the product converted in 6 steps to (3-FC6H4)2CHCH2CHMeNH2. Data for biol. activity of I were given.

IT 186495-49-8P 186495-55-6P 186495-56-7P
186495-99-8P 200429-55-6P 200429-70-5P
200429-72-7P 200430-06-4P 200430-16-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

RN 186495-49-8 CAPLUS

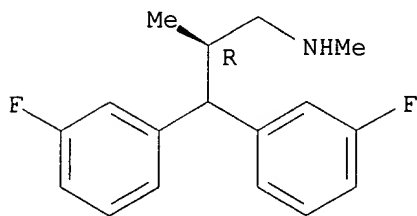
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 186495-55-6 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-,
(β R)- (9CI) (CA INDEX NAME)

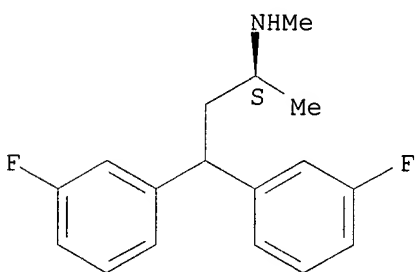
Absolute stereochemistry.



RN 186495-56-7 CAPLUS

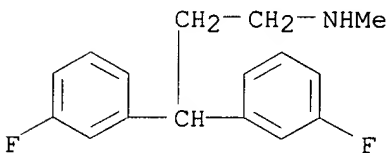
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-,
(α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186495-99-8 CAPLUS

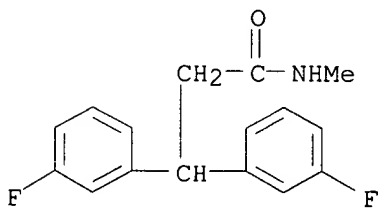
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

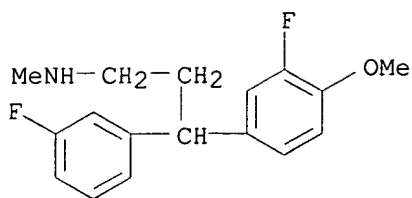
RN 200429-55-6 CAPLUS

CN Benzenepropanamide, 3-fluoro- β -(3-fluorophenyl)-N-methyl- (9CI) (CA
INDEX NAME)



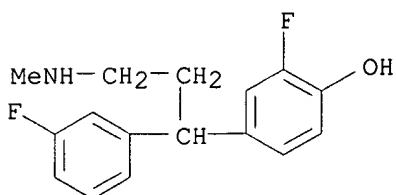
RN 200429-70-5 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-4-methoxy-N-methyl-,
(9CI) (CA INDEX NAME)



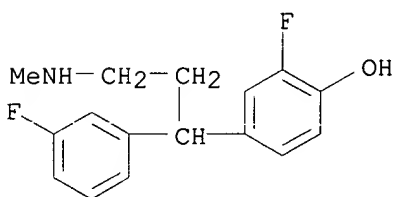
RN 200429-72-7 CAPLUS

CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylanino)propyl]- (9CI) (CA INDEX NAME)



RN 200430-06-4 CAPLUS

CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylanino)propyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

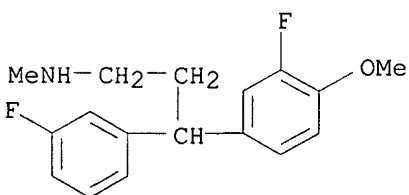
RN 200430-16-6 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 200429-70-5

CMF C17 H19 F2 N O

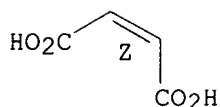


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



IT Calcium channel
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NMDA-binding glutamate receptor complex, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NMDA-binding, calcium channel complexes, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (methyl-D-aspartate-binding, calcium channel complexes, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Cytoprotective agents
 (neuroprotectants; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Analgesics
 Anticonvulsants
 (preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 5586-73-2P, 3,3-Diphenylpropylamine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
 5666-18-2P 14451-09-3P, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
 17349-94-9P 19841-73-7P 21745-77-7P, 9H-Xanthene-9-ethanamine
 21745-81-3P, 9H-Thioxanthene-9-ethanamine 21745-82-4P 21745-83-5P
 21745-85-7P 28075-29-8P 36765-74-9P 48166-95-6P 53179-07-0P
 54910-89-3P 57226-64-9P 63940-51-2P 64630-52-0P 90531-05-8P
 91472-94-5P 95956-62-0P 98383-47-2P 98383-56-3P 106359-50-6P
 109306-10-7P 114754-01-7P 114754-02-8P 114754-03-9P 114754-04-0P
 118468-16-9P 144451-90-1P 144451-98-9P 144452-04-0P 144452-11-9P
 159149-65-2P 170018-54-9P 170018-55-0P 170018-56-1P 170018-57-2P
 170018-63-0P 170018-66-3P 170018-67-4P 170018-68-5P 170018-71-0P
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 170018-82-3P 170018-83-4P 170018-84-5P 170018-85-6P 170018-86-7P
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 186495-41-0P 186495-42-1P 186495-43-2P 186495-44-3P 186495-45-4P
 186495-46-5P 186495-47-6P 186495-48-7P **186495-49-8P**
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| 200429-46-5P | 200429-48-7P | 200429-49-8P | 200429-50-1P | 200429-51-2P |
| 200429-52-3P | 200429-53-4P | 200429-54-5P | 200429-55-6P | |
| 200429-56-7P | 200429-57-8P | 200429-58-9P | 200429-59-0P | 200429-60-3P |
| 200429-61-4P | 200429-62-5P | 200429-63-6P | 200429-64-7P | 200429-65-8P |
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| 200429-71-6P | 200429-72-7P | 200429-73-8P | 200429-74-9P | |
| 200429-75-0P | 200429-76-1P | 200429-77-2P | 200429-78-3P | 200429-79-4P |
| 200429-80-7P | 200429-81-8P | 200429-82-9P | 200429-83-0P | 200429-84-1P |
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| 200429-90-9P | 200429-91-0P | 200429-92-1P | 200429-93-2P | 200429-94-3P |
| 200429-95-4P | 200429-96-5P | 200429-97-6P | 200429-98-7P | 200429-99-8P |
| 200430-00-8P | 200430-01-9P | 200430-02-0P | 200430-03-1P | 200430-04-2P |
| 200430-05-3P | 200430-06-4P | 200430-07-5P | 200430-08-6P | |
| 200430-14-4P | 200430-16-6P | 200430-18-8P | 200430-19-9P | |

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 85-41-6, Phthalimide 103-67-3, N-Methylbenzylamine 135-02-4, o-Anisaldehyde 140-88-5 285-67-6, Cyclopentene oxide 345-70-0, 3,3'-Difluorobenzophenone 351-54-2, 3-Fluoro-p-anisaldehyde 372-20-3, 3-Fluorophenol 452-08-4, 2-Bromo-4-fluoroanisole 456-48-4, 3-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 578-57-4, 2-Bromoanisole 587-04-2, 3-Chlorobenzaldehyde 610-99-1 932-31-0, 2-Methylphenylmagnesium bromide 1073-06-9, 1-Bromo-3-fluorobenzene 1210-35-1, Dibenzosuberone 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one 17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2, (S)-N-Benzyl- α -methylbenzylamine 18707-60-3, Methyl crotonate 20595-30-6, trans-3-Fluorocinnamic acid 21900-39-0, 5-Fluoro-2-methylbenzoyl chloride 65416-24-2, Benzyl crotonate 77532-79-7, 5-Fluoro-2-methylbenzonitrile 100306-34-1 147624-13-3, 3-Fluoro-2-methylbenzaldehyde 170019-09-7, 3,3-Bis(3-fluorophenyl)propionitrile 186496-59-3, 5-Fluoro-2-methylphenylmagnesium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 455-67-4P 458-45-7P 701-38-2P 5561-92-2P, 1-(2-Methoxyphenyl)-1-propanone 15966-37-7P 21745-42-6P 21745-68-6P 25772-94-5P 38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P 156868-83-6P, 3-(3-Fluorophenyl)-1-propanol 170019-11-1P 170019-14-4P, Ethyl 3,3-bis(3-fluorophenyl)propionate 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P 170019-24-6P 170019-25-7P 186496-34-4P 186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P 186496-40-2P 186496-41-3P 186496-42-4P 186496-44-6P 186496-45-7P 186496-46-8P 186496-48-0P 186496-49-1P 186496-50-4P 186496-51-5P 186496-52-6P 186496-53-7P 186496-57-1P 186496-58-2P 186496-60-6P 200430-09-7P 200430-10-0P 200430-11-1P 200430-12-2P, 3,3'-Difluoro-4-methoxybenzophenone 200430-13-3P 200430-15-5P 200430-17-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

L3 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:132773 CAPLUS

DOCUMENT NUMBER: 126:143970

TITLE: Preparation of 1-amino-3,3-diphenylpropanes and related compounds as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system.

INVENTOR(S): Mueller, Alan L.; Moe, Scott T.; Balandrin, Manuel F.; Delmar, Eric G.; Vanwagenen, Bradford C.; Artman, Linda D.; Barmore, Robert M.; Smith, Daryl L.

PATENT ASSIGNEE(S): Nps Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 313 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9640097 | A1 | 19961219 | WO 1996-US10201 | 19960607 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 6071970 | A | 20000606 | US 1995-485038 | 19950607 |
| AU 9661125 | A1 | 19961230 | AU 1996-61125 | 19960607 |
| AU 716122 | B2 | 20000217 | | |
| EP 831799 | A1 | 19980401 | EP 1996-918477 | 19960607 |
| EP 831799 | B1 | 20030502 | | |
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| BR 9609019 | A | 19990706 | BR 1996-9019 | 19960607 |
| NZ 310344 | A | 20010330 | NZ 1996-310344 | 19960607 |
| AT 238782 | E | 20030515 | AT 1996-918477 | 19960607 |
| PL 185492 | B1 | 20030530 | PL 1996-323871 | 19960607 |
| RU 2246300 | C2 | 20050220 | RU 1998-100454 | 19960607 |
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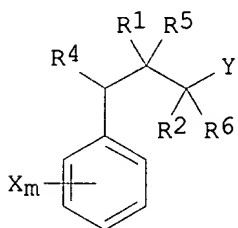
PRIORITY APPLN. INFO.:

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| US 1995-485038 | A | 19950607 |
| US 1993-14813 | B2 | 19930208 |
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| US 1994-288668 | B2 | 19940809 |
| WO 1994-US12293 | A2 | 19941026 |
| WO 1996-US10201 | W | 19960607 |
| AU 1997-13525 | A3 | 19961211 |

OTHER SOURCE(S):

MARPAT 126:143970

GI



AB Title compds. [I; R1, R5 = H, OH, alkyl, hydroxyalkyl, alkoxy, acyloxy, (substituted) Ph, PhCH₂, PhO; R2, R6 = H, alkyl, hydroxyalkyl; R2R4 = imino, (CH₂)_n, (CH₂)_nNR₃(CH₂)_n; R3 = H, alkyl, HOCH₂CH₂, alkylphenyl; n = 0-6, only 1 n can = 0; R4 = (substituted) thiofuryl, pyridyl, Ph, PhCH₂, PhO, PhS; X = (substituted) Ph, PhCH₂, PhO; m = 0-5; Y = N(R₃)₂; when R1R2 = (CH₂)_nNR₃(CH₂)_n, then Y = H], were prepared Thus, di-Et cyanomethylphosphonate was stirred 4 h with NaH in dimethoxyethane; 3,3'-difluorobenzophenone in dimethoxyethane was added and the mixture was stirred 24 h at room temperature to give the cyanomethyl carbinol, which was hydrogenated to give an aminopropanol which was dehydrated and hydrogenated to give 3,3-bis(3-fluorophenyl)propylamine hydrochloride. The latter showed anticonvulsant activity against electroshock-induced seizures in mice with ED₅₀ = 20.1 mg/kg i.p.

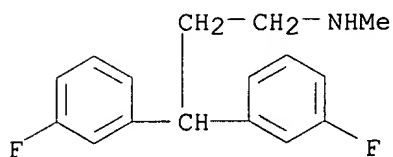
IT 186495-49-8P 186495-55-6P 186495-56-7P
186495-99-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

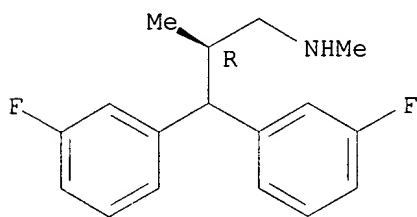
RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



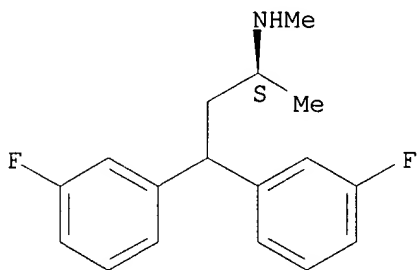
RN 186495-55-6 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-, (β R)- (9CI) (CA INDEX NAME)



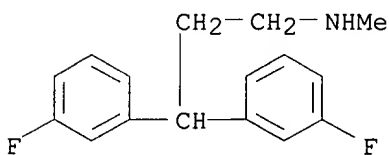
RN 186495-56-7 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-, (α S)- (9CI) (CA INDEX NAME)



RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists

(NMDA antagonists; preparation of 1-amino-3,3-diphenylpropanes and related

compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT Calcium channel

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT Cytoprotective agents

(neuroprotectants; preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT Analgesics

Anticonvulsants

Antihypertensives

Nervous system agents

(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT Brain, disease

(stroke, treatment; preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P

5586-73-2P 5666-18-2P 17349-94-9P 19841-73-7P 28075-29-8P

36765-74-9P 48166-95-6P 53179-07-0P 64630-52-0P 90531-05-8P

91472-94-5P 95956-62-0P 98383-47-2P 98383-56-3P 106359-50-6P

118468-16-9P 144451-90-1P 144451-98-9P 144452-04-0P 144452-11-9P

159149-65-2P 170018-54-9P 170018-55-0P 170018-56-1P 170018-57-2P

170018-63-0P 170018-66-3P 170018-67-4P 170018-68-5P 170018-71-0P

170018-72-1P 170018-73-2P 170018-74-3P 170018-75-4P 170018-76-5P

170018-77-6P 170018-78-7P 170018-79-8P 170018-80-1P 170018-81-2P

170018-82-3P 170018-83-4P 170018-84-5P 170018-85-6P 170018-86-7P

170019-10-0P 186495-37-4P 186495-38-5P 186495-39-6P 186495-40-9P

186495-41-0P 186495-42-1P 186495-43-2P 186495-44-3P 186495-45-4P

186495-46-5P 186495-47-6P 186495-48-7P **186495-49-8P**

186495-50-1P 186495-51-2P 186495-52-3P 186495-53-4P 186495-54-5P

186495-55-6P 186495-56-7P 186495-57-8P 186495-58-9P

186495-59-0P 186495-60-3P 186495-61-4P 186495-62-5P 186495-63-6P

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186495-69-2P 186495-70-5P 186495-71-6P 186495-72-7P 186495-73-8P

186495-74-9P 186495-75-0P 186495-76-1P 186495-77-2P 186495-78-3P

186495-79-4P 186495-80-7P 186495-81-8P 186495-82-9P 186495-83-0P

186495-84-1P 186495-85-2P 186495-86-3P 186495-87-4P 186495-88-5P

186495-89-6P 186495-90-9P 186495-91-0P 186495-92-1P 186495-93-2P

186495-94-3P 186495-95-4P 186495-97-6P 186495-98-7P

186495-99-8P 186496-00-4P 186496-01-5P 186496-02-6P

186496-03-7P 186496-04-8P 186496-05-9P 186496-06-0P 186496-07-1P

186496-08-2P 186496-09-3P 186496-10-6P 186496-11-7P 186496-12-8P

186496-13-9P 186496-14-0P 186496-15-1P 186496-16-2P 186496-17-3P

186496-18-4P 186496-19-5P 186496-20-8P 186496-21-9P 186496-22-0P

186496-23-1P 186496-24-2P 186496-25-3P 186496-26-4P 186496-27-5P

186496-29-7P 186496-30-0P 186496-71-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT 75-16-1, Methylmagnesium bromide 95-46-5, 2-Methylbromobenzene

103-67-3, N-Benzylmethylamine 105-34-0, Methyl cyanoacetate 135-02-4,

2-Methoxybenzaldehyde 140-88-5, Ethyl acrylate 285-67-6, Cyclopentene

oxide 345-70-0, 3,3'-Difluorobenzophenone 372-20-3, 3-Fluorophenol

452-08-4, 2-Bromo-4-fluoroanisole 456-48-4, 3-Fluorobenzaldehyde

529-20-4, 2-Methylbenzaldehyde 578-57-4, 2-Bromoanisole 587-04-2,

3-Chlorobenzaldehyde 867-13-0, Triethyl phosphonoacetate 1073-06-9,

3-Fluorobromobenzene 2627-86-3, (S)- α -Methylbenzylamine

20595-30-6, trans-3-Fluorocinnamic acid 21900-39-0, 5-Fluoro-2-

methylbenzoyl chloride 65416-24-2, Benzyl crotonate 77532-79-7,

5-Fluoro-2-methylbenzonitrile 147624-13-3, 3-Fluoro-2-methylbenzaldehyde

170019-09-7 186496-59-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of 1-amino-3,3-diphenylpropanes and related compds. as
 noncompetitive antagonists of glutamate receptor operated calcium
 channels in the central nervous system)
 IT 455-67-4P 458-45-7P 701-38-2P 1018-97-9P 2537-48-6P, Diethyl
 cyanomethylphosphonate 2845-91-2P 17480-69-2P 25772-94-5P
 38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P
 156868-83-6P 170019-11-1P 170019-12-2P 170019-13-3P 170019-14-4P
 170019-15-5P 170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P
 186496-31-1P 186496-32-2P 186496-33-3P 186496-34-4P 186496-35-5P
 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P 186496-40-2P
 186496-41-3P 186496-42-4P 186496-43-5P 186496-44-6P 186496-45-7P
 186496-46-8P 186496-47-9P 186496-48-0P 186496-49-1P 186496-50-4P
 186496-51-5P 186496-52-6P 186496-53-7P 186496-54-8P 186496-55-9P
 186496-56-0P 186496-57-1P 186496-58-2P 186496-60-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of 1-amino-3,3-diphenylpropanes and related compds. as
 noncompetitive antagonists of glutamate receptor operated calcium
 channels in the central nervous system)

=> file caplus uspatful

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 110.64 | 277.79 |

| | | |
|--|------------|---------|
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -15.00 | -15.00 |

FILE 'CAPLUS' ENTERED AT 22:23:18 ON 03 FEB 2006
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=> s l3
 L4 30 L3

=> dup rem l4
 PROCESSING COMPLETED FOR L4
 L5 27 DUP REM L4 (3 DUPLICATES REMOVED)

=> d ibib abs hitstr 1-27 it

L5 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1315386 CAPLUS
 DOCUMENT NUMBER: 144:45521
 TITLE: Dual-acting serotonin-norepinephrine reuptake
 inhibitor (SNRI)-NMDA antagonists for the treatment of
 genitourinary disorders
 INVENTOR(S): Thor, Karl Bruce
 PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 169 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2005117872 | A2 | 20051215 | WO 2005-US22897 | 20050603 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, | | | | |

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
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 ZA, ZM, ZW

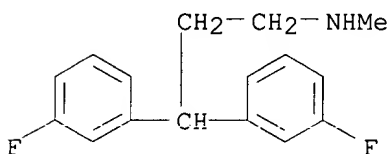
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

US 2005282859 A1 20051222 US 2005-145022 20050603
 PRIORITY APPLN. INFO.: US 2004-576999P P 20040604
 US 2004-607820P P 20040907
 US 2004-640105P P 20041228

AB Comps. and methods are discloses for treatment of genitourinary disorders
 (e.g., urge incontinence). The comps. may generally include a
 dual-acting SNRI-NMDA antagonist (e.g., bicipadine and/or milnacipran).
 Alternatively, the comps. may generally include an SNRI and an NMDA
 antagonist.

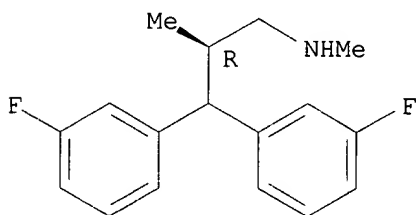
IT **186495-49-8 186495-55-6 186495-56-7**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)

RN 186495-49-8 CAPLUS
 CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA
 INDEX NAME)



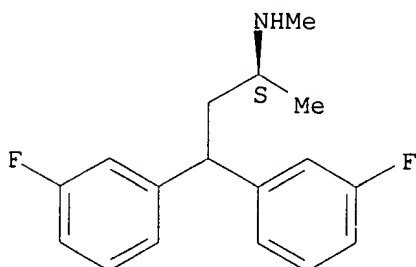
RN 186495-55-6 CAPLUS
 CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-,
 (β R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186495-56-7 CAPLUS
 CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-,
 (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT Disease, animal
(Fowler's syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Glutamate antagonists
(NMDA antagonists; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Prostate gland, disease
(benign hyperplasia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Hyperplasia
(benign prostatic; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(buccal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(capsules; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Pain
(chronic pelvic pain syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(controlled-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease
Inflammation
(cystitis, interstitial (cell); dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(delayed release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra
(disease, urethritis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT 5-HT reuptake inhibitors
Analgesics
Anti-inflammatory agents
Antitumor agents
Bladder, disease
Combination chemotherapy
Drug delivery systems
Human
Neoplasm
Urogenital system, disease
(dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease
(hyperreflexia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease
(incontinence; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(inhalants; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(intravesical; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(mucosal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Nervous system agents
(noradrenaline reuptake inhibitors; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(oral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA

antagonists for treatment of genitourinary disorders)

IT Testis
(orchialgia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease
(overactive bladder, including overactive bladder with sphincter dysfunction; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Disease, animal
(pelvic hypersensitivity or sphincteric spasticity; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Prostate gland, disease
(prostadynia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Inflammation
Prostate gland, disease
(prostatitis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(pulsatile-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(rectal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder
(smooth muscle; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Muscle
(smooth, urinary bladder; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(sublingual; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(sustained-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(tablets; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(transdermal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(transurethral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra
(urethra stricture disease; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Inflammation
(urethritis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Reproductive system
(vulva, vulvodynia or vulvar vestibulitis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT 5586-73-2 14451-09-3, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
21745-77-7, 9H-Xanthene-9-ethanamine 21745-81-3, 9H-Thioxanthene-9-ethanamine 21745-82-4 21745-85-7 28075-29-8 57226-64-9
63106-93-4 63940-51-2 66504-40-3 69096-48-6 71195-57-8
92623-85-3 105310-27-8 109306-10-7 136090-96-5 136090-97-6
144451-98-9 153275-06-0 170018-66-3 170018-67-4 170018-79-8
170018-83-4 186495-47-6 186495-48-7 **186495-49-8**
186495-52-3 186495-53-4 186495-54-5 **186495-55-6**
186495-56-7 186495-66-9 186495-67-0 186495-80-7
186495-84-1 186495-86-3 186495-87-4 186495-88-5 186495-89-6
186495-90-9 186496-20-8 186496-23-1 186496-29-7 186496-30-0
186496-71-9 200429-73-8 200429-74-9 200429-75-0 200429-79-4

| | | | | |
|-------------|-------------|-------------|-------------|-------------|
| 200429-80-7 | 200429-81-8 | 200429-82-9 | 200429-83-0 | 200429-84-1 |
| 200429-85-2 | 200429-86-3 | 200429-87-4 | 255039-66-8 | 255039-67-9 |
| 255039-68-0 | 255039-69-1 | 255039-71-5 | 255039-73-7 | 255039-75-9 |
| 255039-77-1 | 255039-79-3 | 255039-81-7 | 255040-00-7 | 255040-01-8 |
| 255040-02-9 | 255040-03-0 | 255040-04-1 | 255040-05-2 | 255040-07-4 |
| 255040-08-5 | 410074-73-6 | 410074-75-8 | 435293-68-8 | 688738-11-6 |
| 688738-12-7 | 871100-17-3 | 871100-18-4 | 871100-19-5 | 871100-20-8 |
| 871100-21-9 | 871100-22-0 | 871100-23-1 | 871331-21-4 | 871331-22-5 |
| 871331-23-6 | 871331-24-7 | 871331-25-8 | | |

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
antagonists for treatment of genitourinary disorders)

L5 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409336 CAPLUS
DOCUMENT NUMBER: 142:457117
TITLE: Neuroprotective effects of gly-pro-glu following
intravenous infusion
INVENTOR(S): Guan, Jian; Thomas, Gregory Brian; Batchelor, David
Charles; Gluckman, Peter David
PATENT ASSIGNEE(S): Neuren Pharmaceuticals Ltd., N. Z.; Neuren
Pharmaceuticals Inc.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2005042000 | A1 | 20050512 | WO 2004-US35165 | 20041022 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2003-513851P P 20031023
US 2003-515397P P 20031028
US 2004-553688P P 20040316

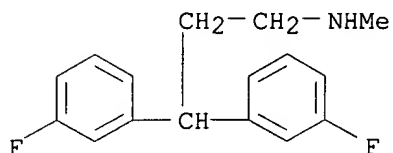
AB Gly-Pro-Glu (GPE) is rapidly metabolized in vivo. We found that GPE
infusion elicits potent and consistent neuroprotection in all brain
regions examined, and in certain embodiments, the effects were greater than
those of a bolus injection followed by infusion ('loading dose/infusion').
GPE reduced apoptosis in the hippocampus and inhibited microglial
proliferation and prevented the injury-induced loss of astrocytes and
improved long-term somatofunction. GPE after infusion showed a broad ED
range (0.3-30mg/kg/h) and had a surprisingly extended window of treatment
efficacy, permitting its use from 1 to at least as late as 24 h after
neural injury. We also found that neuroprotective effects of acute GPE
administration were prolonged and therefore capable of being used
effectively to treat a variety of neurodegenerative conditions, even when
administered after a neural injury. Thus, GPE can be an effective
neuroprotective agent used either alone or co-administered along with
other neuroprotective agents, antiinflammatory agents or peptidase or
protease inhibitors. Compns. of GPE and protease and/or peptidase
inhibitors are provided.

IT 186495-99-8, NPS 1506

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(neuroprotective effects of gly-pro-glu following i.v. infusion)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(2; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT AIDS (disease)
(AIDS dementia complex; neuroprotective effects of gly-pro-glu
following i.v. infusion)

IT Mental and behavioral disorders
(AIDS dementia; neuroprotective effects of gly-pro-glu following i.v.
infusion)

IT Brain, disease
Prion diseases
(Creutzfeldt-Jakob; neuroprotective effects of gly-pro-glu following
i.v. infusion)

IT Growth factors, animal
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(Glial activating factor; neuroprotective effects of gly-pro-glu
following i.v. infusion)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(HSTF1; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Nervous system, disease
(Huntington's chorea; neuroprotective effects of gly-pro-glu following
i.v. infusion)

IT Insulin-like growth factor-binding proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(IGFBP-3; neuroprotective effects of gly-pro-glu following i.v.
infusion)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LPAM-1 (lymphocyte Peyer's patch adhesion mol. 1); neuroprotective
effects of gly-pro-glu following i.v. infusion)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(MAdCAM-1; neuroprotective effects of gly-pro-glu following i.v.
infusion)

IT Brain, disease
(Schilder's disease; neuroprotective effects of gly-pro-glu following
i.v. infusion)

IT Nervous system, disease
(amyotrophic lateral sclerosis; neuroprotective effects of gly-pro-glu
following i.v. infusion)

IT Brain
(cerebral cortex; neuroprotective effects of gly-pro-glu following i.v.
infusion)

IT Ischemia
(cerebral; neuroprotective effects of gly-pro-glu following i.v.
infusion)

IT Encephalomyelitis

(chronic relapsing; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Surgery
(coronary artery bypass; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Artery
(coronary, bypass surgery; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain
(corpus striatum; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Radiation
(damage; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Nerve, disease
(death; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Nerve, disease
Nervous system, disease
(degeneration; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Central nervous system, disease
(demyelination; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain
(dentate gyrus; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Mental and behavioral disorders
(depression; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Surgery
(elective; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Neurotrophic factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glial-derived; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Injury
(head and neck; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain
(hippocampus, sector CA1; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain
(hippocampus, sector CA2; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain
(hippocampus, sector CA3; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain
(hippocampus, sector CA4; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Drug delivery systems
(infusions, i.v.; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Head and Neck, disease
Nerve, disease
Reperfusion
(injury; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Gene, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(int-2; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain, disease
Nerve, disease
(ischemia; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain, disease

(leukoencephalopathy; neuroprotective effects of gly-pro-glu following i.v. infusion)

- IT Neuroglia
 - (microglia; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Inflammation
 - Spinal cord, disease
 - (myelitis; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Inflammation
 - Nerve, disease
 - (neuritis; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Nerve, neoplasm
 - (neuroblastoma; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Cell death
 - (neuron; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Injury
 - Ischemia
 - (neuronal; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Alzheimer's disease
 - Anti-Alzheimer's agents
 - Anti-inflammatory agents
 - Anticonvulsants
 - Antidepressants
 - Antiparkinsonian agents
 - Antipsychotics
 - Asphyxia
 - Astrocyte
 - Down's syndrome
 - Encephalitis
 - Encephalomyelitis
 - Epilepsy
 - Hypoxia
 - Inflammation
 - Leukemia
 - Meningitis
 - Multiple sclerosis
 - Parkinson's disease
 - Schizophrenia
 - Spinal muscular atrophy
 - (neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Toxins
 - RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 - (neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Cytokines
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Proliferating cell nuclear antigen
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Insulin-like growth factor-binding proteins
 - Interleukins
 - Neurotrophic factors
 - Tumor necrosis factors
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Cytoprotective agents
 - (neuroprotective; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Nervous system, disease
 - (optic neuromyelitis; neuroprotective effects of gly-pro-glu following i.v. infusion)
- IT Nerve, disease
 - (peripheral neuropathy; neuroprotective effects of gly-pro-glu

following i.v. infusion)

IT Brain, disease
(progressive multifocal leukoencephalopathy; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Paralysis
(pseudobulbar; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Injury
(reperfusion; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatotropin-binding; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain, disease
Brain, disease
(stroke; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain, disease
(trauma; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α ; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha 4\beta 1$; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
($\beta 1$ -; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β ; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ ; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT 9001-92-7, Proteinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT 9015-82-1, Peptidyl dipeptidase 9031-94-1, Aminopeptidase 9031-98-5, Carboxypeptidase 9031-99-6, Dipeptidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT 56-40-6, Glycine, biological studies 56-86-0, L-Glutamic acid, biological studies 147-85-3, Proline, biological studies 704-15-4
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(neuroprotective effects of gly-pro-glu following i.v. infusion)

IT 37205-61-1, Proteinase inhibitor 37259-58-8, Serine protease 37353-41-6, Cysteine protease 123584-45-2, Fibroblast growth factor 4 130939-41-2, Fibroblast growth factor 6 145266-99-5, Metalloproteinase inhibitor 148348-14-5, Fibroblast growth factor 3 169592-56-7, Caspase-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuroprotective effects of gly-pro-glu following i.v. infusion)

IT 32302-76-4
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP

(Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (neuroprotective effects of gly-pro-glu following i.v. infusion)
 IT 492-27-3, Kynurenic acid 533-45-9, Clomethiazole 9002-72-6, Growth hormone 9061-61-4, Nerve growth factor 9087-70-1, Aprotinin 14611-51-9, Selegiline 26305-03-3, Pepstatin A 30827-99-7, AEBSF 50913-82-1, ORG 2766 55123-66-5, Leupeptin 58970-76-6, Bestatin 66701-25-5 67763-96-6, IGF-1 67763-97-7, IGF-II 77086-22-7, MK-801 80714-61-0, Semax 104987-11-3, Tacrolimus 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 106956-32-5, Oncostatin M 114949-22-3, Activin 118876-58-7, NBQX 130939-66-1, Neurotrophin 3 143375-33-1, Neurotrophin 4 148348-15-6, Keratinocyte growth factors 161832-65-1, LY 300164 161832-71-9, LY 303070 171758-70-6, Keratinocyte growth factor 2 **186495-99-8**, NPS 1506 204719-95-9, Fibroblast growth factor 16 524706-48-7, GV 1505260
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (neuroprotective effects of gly-pro-glu following i.v. infusion)
 REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 27 USPATFULL on STN
 ACCESSION NUMBER: 2005:324947 USPATFULL
 TITLE: Dual acting SNRI-NMDA antagonists for the treatment of genitourinary disorders
 INVENTOR(S): Thor, Karl Bruce, Cary, NC, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2005282859 | A1 | 20051222 |
| APPLICATION INFO.: | US 2005-145022 | A1 | 20050603 (11) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2004-576999P | 20040604 (60) |
| | US 2004-607820P | 20040907 (60) |
| | US 2004-640105P | 20041228 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109, US | |
| NUMBER OF CLAIMS: | 92 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 6 Drawing Page(s) | |
| LINE COUNT: | 4912 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are compositions and methods for treatment of genitourinary disorders (e.g., urge incontinence). The compositions may generally include a dual-acting SNRI-NMDA antagonist (e.g., bicifadine and/or milnacipran). Alternatively, the compositions may generally include an SNRI and an NMDA antagonist.

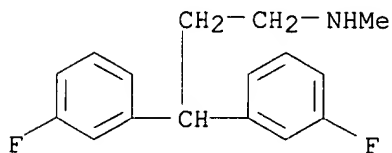
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **186495-49-8 186495-55-6 186495-56-7**

(dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

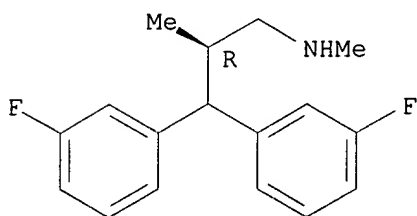
RN 186495-49-8 USPATFULL

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



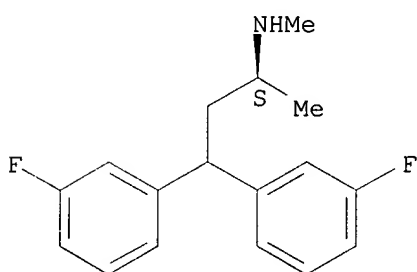
RN 186495-55-6 USPATFULL
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-,
(β R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186495-56-7 USPATFULL
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-,
(α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT Disease, animal
(Fowler's syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Glutamate antagonists
(NMDA antagonists; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Prostate gland, disease
(benign hyperplasia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Hyperplasia
(benign prostatic; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(buccal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(capsules; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Pain
(chronic pelvic pain syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(controlled-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease

IT Inflammation
(cystitis, interstitial (cell); dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(delayed release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra
(disease, urethritis; dual-acting serotonin-norepinephrine reuptake

inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT 5-HT reuptake inhibitors
 IT Analgesics
 IT Anti-inflammatory agents
 IT Antitumor agents
 IT Bladder, disease
 IT Combination chemotherapy
 IT Drug delivery systems
 IT Human
 IT Neoplasm
 IT Urogenital system, disease
 (dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
 IT Bladder, disease
 (hyperreflexia; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Bladder, disease
 (incontinence; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems
 (inhalants; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems
 (intravesical; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems
 (mucosal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
 IT Nervous system agents
 (noradrenaline reuptake inhibitors; dual-acting serotonin-
 norepinephrine reuptake inhibitor-NMDA antagonists for treatment of
 genitourinary disorders)
 IT Drug delivery systems
 (oral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
 IT Testis
 (orchialgia; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Bladder, disease
 (overactive bladder, including overactive bladder with sphincter
 dysfunction; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Disease, animal
 (pelvic hypersensitivity or sphincteric spasticity; dual-acting
 serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for
 treatment of genitourinary disorders)
 IT Prostate gland, disease
 (prostodynia; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Inflammation
 IT Prostate gland, disease
 (prostatitis; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems
 (pulsatile-release; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems
 (rectal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
 antagonists for treatment of genitourinary disorders)
 IT Bladder
 (smooth muscle; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Muscle
 (smooth, urinary bladder; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems
 (sublingual; dual-acting serotonin-norepinephrine reuptake
 inhibitor-NMDA antagonists for treatment of genitourinary disorders)
 IT Drug delivery systems

(sustained-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(tablets; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(transdermal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems
(transurethral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra
(urethra stricture disease; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Inflammation
(urethritis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Reproductive system
(vulva, vulvodynia or vulvar vestibulitis; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT 5586-73-2 14451-09-3, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
21745-77-7, 9H-Xanthene-9-ethanamine 21745-81-3, 9H-Thioxanthene-9-ethanamine 21745-82-4 21745-85-7 28075-29-8 57226-64-9
63106-93-4 63940-51-2 66504-40-3 69096-48-6 71195-57-8
92623-85-3 105310-27-8 109306-10-7 136090-96-5 136090-97-6
144451-98-9 153275-06-0 170018-66-3 170018-67-4 170018-79-8
170018-83-4 186495-47-6 186495-48-7 **186495-49-8**
186495-52-3 186495-53-4 186495-54-5 **186495-55-6**
186495-56-7 186495-66-9 186495-67-0 186495-80-7
186495-84-1 186495-86-3 186495-87-4 186495-88-5 186495-89-6
186495-90-9 186496-20-8 186496-23-1 186496-29-7 186496-30-0
186496-71-9 200429-73-8 200429-74-9 200429-75-0 200429-79-4
200429-80-7 200429-81-8 200429-82-9 200429-83-0 200429-84-1
200429-85-2 200429-86-3 200429-87-4 255039-66-8 255039-67-9
255039-68-0 255039-69-1 255039-71-5 255039-73-7 255039-75-9
255039-77-1 255039-79-3 255039-81-7 255040-00-7 255040-01-8
255040-02-9 255040-03-0 255040-04-1 255040-05-2 255040-07-4
255040-08-5 410074-73-6 410074-75-8 435293-68-8 688738-11-6
688738-12-7 871100-17-3 871100-18-4 871100-19-5 871100-20-8
871100-21-9 871100-22-0 871100-23-1 871331-21-4 871331-22-5
871331-23-6 871331-24-7 871331-25-8
(dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

L5 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2004:353140 CAPLUS

DOCUMENT NUMBER: 140:380634

TITLE: Compositions of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for the treatment or prevention of neuropathic pain

INVENTOR(S): Cheung, Raymond Y.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004082543 | A1 | 20040429 | US 2002-282660 | 20021029 |
| WO 2004039371 | A2 | 20040513 | WO 2003-US33089 | 20031017 |
| WO 2004039371 | A3 | 20040617 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-282660 A 20021029

OTHER SOURCE(S): MARPAT 140:380634

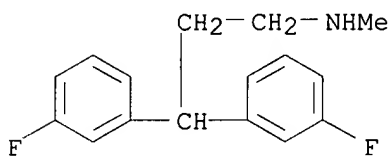
AB The present invention provides compns. and methods to treat or prevent neuropathic pain in a subject using a combination of a COX-2 selective inhibitor and a NMDA receptor antagonist.

IT **186495-49-8**, Delucemine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT Glutamate receptors

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NMDA-binding; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

IT Pain

(neuropathic; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

IT Nerve, disease

(neuropathy, related pain, treatment of; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

IT Drug delivery systems

(prodrugs; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

IT 329900-75-6, COX-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (COX-2; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

IT 52-52-8, 1-Aminocyclopentane-carboxylic acid 56-40-6, Glycine, biological studies 83-98-7, Orphenadrine 125-71-3, Dextromethorphan 254-04-6, 2H-1-Benzopyran 726-99-8, Fluorofelbamate 768-94-5, Amantadine 6740-88-1, Ketamine 19982-08-2, Memantine 25451-15-4, Felbamate 57982-78-2, Budipine 68134-81-6, Gacyclidine 70172-33-7 71125-38-7, Meloxicam 92623-85-3, Milnacipran 93438-65-4, Conantokin G 96206-92-7, 2-Methyl-6-(phenylethynyl)-pyridine 97240-79-4, Topiramate 104454-71-9, Ipenoxazone 112924-45-5, Dexanabinol 117414-74-1, Midafotel 117571-54-7 120667-19-8 123653-11-2, {N-[2-(Cyclohexyloxy)-4-nitrophenyl]methanesulfonamide} 128298-28-2, Remacemide 132472-31-2 134234-12-1, Traxoprodil 135025-56-8, 7-Chlorothiokynurenic acid 136109-04-1 137159-92-3, Aptiganel 138047-56-0 139051-78-8 142235-88-9 143850-75-3 144912-63-0 153322-05-5, Lanicemine 153504-81-5, Licostinel 160754-76-7 161230-88-2 161292-39-3 162011-90-7, Rofecoxib 166974-22-7 169590-41-4, Deracoxib 169590-42-5, Celecoxib 170029-85-3 173186-99-7 180200-68-4, 4-(4-Cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide 181695-72-7, Valdecocixib **186495-49-8**, Delucemine 193278-48-7 193356-17-1 197077-52-4 198470-84-7, Parecoxib 198710-92-8, Kaitocephalin 200430-63-3 202409-33-4, Etoricoxib 202807-80-5 202914-18-9 212126-32-4, 2-(3,5-Difluorophenyl)-3-[4-

(methylsulfonyl)phenyl}-2-cyclopenten-1-one 219810-59-0, Neramexane
252374-41-7 253450-09-8, Besonprodil 266320-83-6, ABT 963
342047-49-8 369640-27-7 676451-52-8D, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comps. of cyclooxygenase-2 selective inhibitors and NMDA receptor
antagonists for treatment or prevention of neuropathic pain)

L5 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1059129 CAPLUS

DOCUMENT NUMBER: 142:32998

TITLE: Compositions of a cyclooxygenase-2 selective inhibitor
and a cannabinoid agent for the treatment of central
nervous system damage

INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 177 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2004105699 | A2 | 20041209 | WO 2004-US16496 | 20040526 |
| WO 2004105699 | A3 | 20051215 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-473820P P 20030528

OTHER SOURCE(S): MARPAT 142:32998

AB The present invention provides comps. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a cannabinoid agent in combination with a cyclooxygenase-2 selective inhibitor.

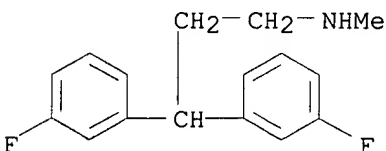
IT **186495-49-8**, Delucemine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comps. of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT Ischemia

(central nervous system; comps. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Combination chemotherapy

Drug interactions

Ischemia
 (compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Cannabinoids
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Central nervous system, disease
 (ischemia; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Cytoprotective agents
 (neuroprotective; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Brain, disease
 (stroke; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT 52-52-8, 1-Aminocyclopentanecarboxylic acid 56-40-6, Glycine, biological studies 83-98-7, Orphenadrine 521-35-7, Cannabinol 726-99-8, Fluorofelbamate 1972-08-3, Dronabinol 7541-16-4 13956-29-1, Cannabidiol 25451-15-4, Felbamate 35377-89-0, 1-Methoxy-endo-4-hydroxy-9-oxabicyclo[3.3.1]nonane 38964-50-0 53847-30-6, 2-Arachidonylglycerol 57982-78-2, Budipine 68134-81-6, Gacyclidine 71125-38-7, Meloxicam 76163-84-3 76163-85-4 76163-87-6 76163-88-7 80286-75-5 83002-04-4 92623-85-3, Milnacipran 93438-65-4, Conantokin G 96206-92-7, 2-Methyl-6-(phenylethynyl)pyridine 97240-79-4, Topiramate 104454-71-9, Ipenoxazone 112924-45-5, Dexanabinol 117414-74-1, Midafotel 117571-54-7 119784-07-5 120667-19-8 123653-11-2, N-[2-(Cyclohexyloxy)-4-nitrophenyl]methanesulfonamide 124649-81-6 128298-28-2, Remacemide 132472-31-2 135025-56-8, 7-Chlorothiokynurenic acid 136109-04-1 137159-92-3, Aptiganel 138047-56-0 139051-78-8 140835-14-9 142235-88-9 143850-75-3 144912-63-0 153322-05-5, Lanicemine 153504-81-5, Licostinel 155471-08-2 157182-49-5 158328-22-4 160754-76-7 161230-88-2 161292-39-3 162011-90-7, Rofecoxib 164178-33-0 166974-22-7 168273-06-1 169590-41-4, Deracoxib 169590-42-5, Celecoxib 173186-99-7 176977-56-3, [6-Methoxy-2-(4-methoxyphenyl)benzo[b]furan-3-yl](4-cyanophenyl)methanone 180200-68-4, 4-(4-Cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide 181695-72-7, Valdecocixib 183232-66-8 **186495-49-8**, Delucemine 192703-06-3 193278-48-7 193356-17-1 197077-52-4 197438-41-8 198470-84-7, Parecoxib 198710-92-8, Kaitocephalin 200430-63-3 202409-33-4, Etoricocixib 202463-68-1 202807-80-5 202914-18-9 212126-32-4, 2-(3,5-Difluorophenyl)-3-[4-(methylsulfonyl)phenyl]-2-cyclopenten-1-one 215123-80-1 219810-59-0, Neramexane 220991-20-8, Lumiracocixib 220991-33-3 252374-41-7 253450-09-8, Besonprodil 256510-26-6 266320-83-6 342047-49-8 369640-27-7 803731-69-3 803731-70-6 803731-71-7
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compns. of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT 329900-75-6, Cyclooxygenase 2 329967-85-3, Cyclooxygenase-1
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

L5 ANSWER 6 OF 27 USPATFULL on STN
 ACCESSION NUMBER: 2004:51583 USPATFULL
 TITLE: Methods and compounds for treating depression and other disorders
 INVENTOR(S): Mueller, Alan L., Salt Lake City, UT, UNITED STATES
 Moe, Scott T., Salt Lake City, UT, UNITED STATES
 Balandrin, Manuel F., Sandy, UT, UNITED STATES
 PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc. (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|---------------|------|----------|
| PATENT INFORMATION: | US 2004039014 | A1 | 20040226 |

APPLICATION INFO.: US 2001-990405 A1 20011121 (9)
RELATED APPLN. INFO.: Continuation of Ser. No. WO 1999-US15857, filed on 12
Jul 1999, UNKNOWN

| | NUMBER | DATE |
|--|---|---------------|
| PRIORITY INFORMATION: | US 1998-92546P | 19980713 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | FOLEY & LARDNER, 402 WEST BROADWAY, 23RD FLOOR, SAN DIEGO, CA, 92101 | |
| NUMBER OF CLAIMS: | 18 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 1998 | |
| CAS INDEXING IS AVAILABLE FOR THIS PATENT. | | |

AB The present invention features compounds active at both the serotonin reuptake site and the N-methyl-D-aspartate (NMDA) receptor and the use of such compounds for treating different disorders. Compounds having activity at the serotonin reuptake site and the NMDA receptor ("multi-active compounds") can be used to treat different types of disorders such as depression, obsessive-compulsive disorders (OCD), sleep, disorders, sexual dysfunction, and eating disorders. Preferably, the multi-active compounds are used to treat depression.

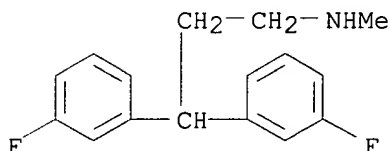
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **186495-99-8P**

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

RN 186495-99-8 USPATFULL

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists

(NMDA antagonists; preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT Antidepressants

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 5-HT receptors

(reuptake inhibitors; preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 21745-82-4P 21745-83-5P 50366-32-0P 186495-87-4P

186495-99-8P 186496-01-5P 200429-75-0P 200430-07-5P

255039-63-5P 255039-64-6P 255039-65-7P 255039-66-8P 255039-67-9P

255039-68-0P 255039-69-1P 255039-70-4P 255039-71-5P 255039-72-6P

255039-73-7P 255039-74-8P 255039-75-9P 255039-76-0P 255039-77-1P

255039-78-2P 255039-79-3P 255039-80-6P 255039-81-7P 255039-82-8P

255040-00-7P 255040-01-8P 255040-02-9P 255040-03-0P 255040-04-1P

255040-05-2P 255040-07-4P 255040-08-5P

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

IT 74-89-5, Methylamine, reactions 95-48-7, reactions 103-67-3,
N-Benzylmethylamine 140-88-5 345-69-7, 3-Fluorobenzophenone
345-70-0, 3,3'-Difluorobenzophenone 372-20-3, 3-Fluorophenol
395-23-3, 4-Trifluoromethylbenzhydrol 402-45-9, p-Trifluoromethylphenol
457-68-1, 4,4'-Difluorodiphenylmethane 529-20-4, o-Tolualdehyde
540-51-2, 2-Bromoethanol 590-17-0, Bromoacetonitrile 625-36-5,
3-Chloropropionyl chloride 932-31-0, o-Tolylmagnesium bromide
933-88-0, o-Toluoyl chloride 1073-06-9, 3-Bromofluorobenzene
1210-35-1, Dibenzosuberone 2537-48-6, Diethyl cyanomethylphosphonate
20595-30-6, trans-3-Fluorocinnamic acid 72551-53-2 100306-33-0
100306-34-1 186496-23-1

(preparation of diarylalkylamines and related compds. active at both the
serotonin reuptake site and the N-methyl-D-aspartate receptor for
treatment depression and other disorders)

IT 365-17-3P 458-45-7P 1018-97-9P 15966-37-7P 25772-94-5P
38158-75-7P 50499-52-0P 53915-75-6P 69096-48-6P 83406-26-2P
84648-43-1P 98586-21-1P 156868-83-6P 186496-49-1P 186496-50-4P
186496-57-1P 186496-58-2P 186496-60-6P 200430-09-7P 200430-10-0P
200430-17-7P 255039-83-9P 255039-84-0P 255039-85-1P 255039-86-2P
255039-87-3P 255039-88-4P 255039-89-5P 255039-90-8P 255039-91-9P
255039-92-0P 255039-93-1P 255039-94-2P 255039-95-3P 255039-96-4P
255039-97-5P 255039-98-6P 255039-99-7P

(preparation of diarylalkylamines and related compds. active at both the
serotonin reuptake site and the N-methyl-D-aspartate receptor for
treatment depression and other disorders)

L5 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:781548 CAPLUS

DOCUMENT NUMBER: 141:254405

TITLE: Acute treatment with MgSO4 attenuates long-term
hippocampal tissue loss after brain trauma in the rat
AUTHOR(S): Browne, Kevin D.; Leon, Matthew J.; Iwata, Akira;
Chen, Xiao-Han; Smith, Douglas H.

CORPORATE SOURCE: Department of Neurosurgery, University of
Pennsylvania, Philadelphia, PA, USA

SOURCE: Journal of Neuroscience Research (2004), 77(6),
878-883

CODEN: JNREDK; ISSN: 0360-4012

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

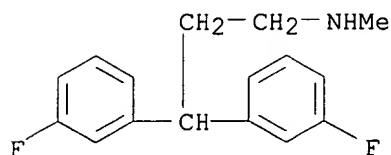
AB Previous studies have shown that magnesium salts and the noncompetitive
N-methyl-D-aspartate (NMDA) receptor antagonist, NPS 1506, attenuated
short-term cognitive deficits and histopathol. changes associated with
traumatic brain injury (TBI). We evaluated the long-term effects of both
therapies after brain trauma. Young adult rats were subjected to
parasagittal fluid-percussion brain injury and received either MgSO4 (125
 μ mol/400 g rat; n = 12) 15 min post-injury, NPS 1506 (1.15 mg/kg; n =
12) 15 min and 4 h post-injury, or vehicle (n = 9) 15 min post-injury.
Uninjured animals (sham) received vehicle (n = 10). Learning function in
these animals was evaluated using a water maze paradigm 8 mo after injury
or sham treatment, and the brains were examined for cortical and hippocampal
tissue loss. Compared to sham animals, injured vehicle-treated animals
displayed a substantial learning dysfunction, indicated by an increased
latency to find a hidden platform in the water maze ($P < 0.001$). No
improvements in learning, however, were found for injured animals treated
with NPS 1506 or MgSO4. Injury induced >30% loss of tissue in the
ipsilateral cortex in vehicle-treated animals that was not reduced in
animals treated with either NPS 1506 or MgSO4. Treatment with MgSO4
significantly reduced progressive tissue loss in the hippocampus ($P <$
0.001). These findings are the first to demonstrate long-term
neuroprotection of hippocampal tissue by an acute treatment in a TBI
model. These data also show that the previously reported broad efficacy
of MgSO4 or NPS 1506 observed shortly after brain trauma could not be
detected 8 mo post-injury.

IT 186495-99-8, NPS 1506

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(MgSO4 attenuates long-term hippocampal tissue loss after brain trauma)

in rat)
 RN 186495-99-8 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
 hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Cognition
 Learning disorders
 (MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)
 IT Glutamate antagonists
 (NMDA antagonists; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)
 IT Brain
 (cortex; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)
 IT Brain
 (hippocampus, atrophy; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)
 IT Cytoprotective agents
 (neuroprotective; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)
 IT Brain, disease
 (trauma; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)
 IT 7487-88-9, Sulfuric acid magnesium salt (1:1), biological studies
186495-99-8, NPS 1506
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:396671 CAPLUS
 DOCUMENT NUMBER: 138:379256
 TITLE: Cyclic prolylglycine composition and therapeutic uses
 INVENTOR(S): Tran, Loi
 PATENT ASSIGNEE(S): USA
 SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2003041655 | A2 | 20030522 | WO 2002-US36639 | 20021112 |
| WO 2003041655 | A3 | 20040910 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2466701 AA 20030522 CA 2002-2466701 20021112
US 2003109531 A1 20030612 US 2002-292732 20021112
NZ 2001-515432 A 20011113
US 2002-405909P P 20020826
WO 2002-US36639 W 20021112

PRIORITY APPLN. INFO.:

AB The invention discloses compns. containing, and use of, cyclic prolylglycine, and analogs and mimetics thereof, as neuroprotective agents for the treatment and or prevention of neurol. disorders including but not limited to cerebral ischemia or cerebral infarction resulting from a range of phenomena, e.g. thromboembolic or hemorrhagic stroke, cerebral basospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia (e.g. from drowning), pulmonary surgery, and cerebral trauma, as well as the treatment and prevention of chronic neurodegenerative disorders, e.g. Alzheimer's disease, Parkinson's disease, and Huntington's disease, and use as anticonvulsants.

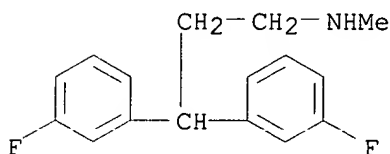
IT 186495-99-8, NPS 1506

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclic prolylglycine composition and therapeutic uses, and use with other agents)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Bone morphogenetic proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(2; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Glutamate receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(AMPA-binding, antagonists; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT CD antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(CD106, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT CD antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(CD11A, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT CD antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(CD18, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(FHF-1; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
 (FHF-2; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (FHF-3; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (FHF-4; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Nervous system, disease
 (Huntington's chorea; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ICAM (intercellular adhesion mol.), agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (LPAM-1 (lymphocyte Peyer's patch adhesion mol. 1), agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (Leu-CAM (leukocytic cell adhesion mol.), agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (MAdCAM-1 (mucosal addressin cell adhesion mol.-1), agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Tumor necrosis factors
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (TNF- α ; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (VCAM-1 (vascular cell adhesion mol. 1), agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cerebrospinal fluid
 (artificial; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain
 (cerebellum, neurons; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Injury
 (cerebral; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Interferons
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (consensus~~x~~; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Surgery
 (coronary artery bypass, neurol. injury from; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Artery
 (coronary, bypass surgery, neurol. injury from; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Alzheimer's disease
 Anti-Alzheimer's agents
 Anti-inflammatory agents
 Antiparkinsonian agents
 Apoptosis
 Drug delivery systems

- Encephalomyelitis
- Glutamate antagonists
- Inflammation
- Multiple sclerosis
- Myelination
- Nerve
- Nerve, disease
- Nerve regeneration
- Nerve regeneration
- Nervous system agents
- Neuroglia
- Neuron
- Neurotoxicity
- Parkinson's disease
- Peptidomimetics
 - (cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Ciliary neurotrophic factor
- Insulin-like growth factor-binding proteins
- Interleukins
- Leukemia inhibitory factor
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
 - (cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Nerve, disease
 - (death; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Nervous system, disease
 - (degeneration; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Neurotrophic factors
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
 - (glial-derived; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Proteins
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
 - (hst/Kfgk gene product; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Drug delivery systems
 - (inhalants; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Drug delivery systems
 - (injections, i.m.; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Drug delivery systems
 - (injections, i.p.; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Drug delivery systems
 - (injections, i.v.; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Drug delivery systems
 - (injections, s.c.; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Drug delivery systems
 - (injections; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Brain, disease
- Nerve, disease
 - (injury; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Proteins
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
 - (int-2; cyclic prolylglycine composition and therapeutic uses, and use with other agents)
- IT Brain, disease

(leucodystrophy; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Glutamate receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (metabotropic, mGluR2; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Glutamate receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (metabotropic, mGluR3; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Antibodies and Immunoglobulins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (monoclonal, MECA-367; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Axon
 (myelination; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Inflammation
 Spinal cord, disease
 (myelitis, transverse; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Drug delivery systems
 (nasal; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Encephalitis
 (necrotizing hemorrhagic; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Central nervous system
 (neurogenesis; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Asphyxia
 (neurol. injury from; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Toxins
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (neurol. injury from; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Nervous system, disease
 (neuromyelitis optica; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cell death
 (neuron; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Injury
 (neuronal; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Cytoprotective agents
 (neuroprotective; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain
 (nigrostriatum; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Inflammation
 Nerve, disease
 (optic neuritis; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Drug delivery systems
 (oral; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain
 (pons, central pontine myelinolysis; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain, disease
 (progressive multifocal leukoencephalopathy; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Drug delivery systems
 (rectal; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Nervous system, disease
(sclerosis, diffuse cerebral sclerosis of Schilder; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatotropin-binding; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain, disease
(stroke, neurol. injury from; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Drug delivery systems
(systemic; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain, disease
(trauma; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Brain
(white matter, damage; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(χ ; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α ; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α L, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α 4, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α 4 β 1, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β 1-; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β ; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β 7, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT 492-27-3, Kynurenic acid 533-45-9, Clomethiazole 2578-57-6
2578-57-6D, analogs and peptidomimetics 9002-72-6, Growth hormone
9061-61-4, Nerve growth factor 14611-51-9, Selegiline 50913-82-1, ORG
2766 67763-96-6, Insulin-like growth factor 1 67763-97-7, Insulin-like
growth factor 2 77086-21-6, Dizocilpine 77086-22-7, MK-801
80714-61-0, Semax 104987-11-3, FK506 106096-92-8, Acidic fibroblast
growth factor 106096-93-9, Basic fibroblast growth factor 106956-32-5,
Oncostatin M 109836-81-9, L-threo-1-Phenyl-2-decanoylamino-3-morpholino-
1-propanol 114949-22-3, Activin 118876-58-7, NBQX 123584-45-2,
Fibroblast growth factor 4 130939-41-2, Fibroblast growth factor 6
130939-66-1, Neurotrophin 3 140698-57-3, Activity-dependent neurotrophic
factor 143375-33-1, Neurotrophin 4 148348-14-5, Fibroblast growth
factor 3 148348-15-6, Fibroblast growth factor 7 153436-22-7, GV

150526 161832-65-1, LY300164 161832-71-9, LY303070 171758-70-6,
Fibroblast growth factor 10 **186495-99-8**, NPS 1506 204719-95-9,
Fibroblast growth factor 16 524706-48-7, GV 1505260
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(cyclic prolylglycine composition and therapeutic uses, and use with other
agents)
IT 56-86-0, L-Glutamic acid, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); BIOL (Biological study)
(glutamate toxicity; cyclic prolylglycine composition and therapeutic uses,
and use with other agents)

L5 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:376586 CAPLUS
DOCUMENT NUMBER: 138:379245
TITLE: Cyclo(prolylglycine) and methods of use to treat
neural disorders
INVENTOR(S): Guan, Jian; Gluckman, Peter David; Sieg, Frank
PATENT ASSIGNEE(S): Neuronz Limited, N. Z.; Neuronz Biosciences, Inc.
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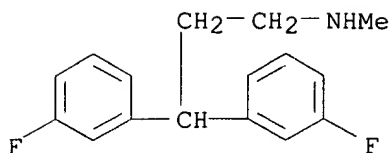
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2003039487 | A2 | 20030515 | WO 2002-US36235 | 20021112 |
| WO 2003039487 | A3 | 20040115 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: NZ 2001-515371 A 20011109
NZ 2001-515432 A 20011113
NZ 2001-515551 A 20011116

AB Embodiments of pharmaceutical compns. comprising cyclo(Pro-Gly) (cPG) and methods for use in treating neural degeneration are provided. The cPG substantially prevents toxic neural degeneration and cell death and promotes neurite outgrowth in neurons, especially cerebellar neurons. The neuroprotective and neuroregenerative effects of cPG are useful to treat behavioral neurol. deficits involving motor control pathways.

IT **186495-99-8**, NPS 1506
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(cyclo(prolylglycine) for treatment of neural disorders, and use with
other agents)

RN 186495-99-8 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

- IT Bone morphogenetic proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Glutamate receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (AMPA-binding, antagonists; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Growth factors, animal
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Androgen-induced growth factor; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT CD antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD106; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT CD antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD11A; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT CD antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD18; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Brain, disease
 Nervous system, disease
 (Devic's disease; cyclo(prolylglycine) for treatment of neural disorders)
- IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (FHF-1; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (FHF-2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (FHF-3; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (FHF-4; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Growth factors, animal
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Glial-activating factor; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)
- IT Nervous system, disease
 (Huntington's chorea; cyclo(prolylglycine) for treatment of neural

disorders)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ICAM (intercellular adhesion mol.); cyclo(prolylglycine) for treatment
 of neural disorders, and use with other agents)

IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (LPAM-1 (lymphocyte Peyer's patch adhesion mol. 1);
 cyclo(prolylglycine) for treatment of neural disorders, and use with
 other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (Leu-CAM (leukocytic cell adhesion mol.); cyclo(prolylglycine) for
 treatment of neural disorders, and use with other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (MAdCAM-1 (mucosal addressin cell adhesion mol.-1);
 cyclo(prolylglycine) for treatment of neural disorders, and use with
 other agents)

IT Nervous system, disease
 (Machado-Joseph; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Neuron
 (Purkinje cell, 5-fluorouracil- or cytosine arabinoside-induced loss of
 Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)

IT Tumor necrosis factors
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (TNF- α ; cyclo(prolylglycine) for treatment of neural disorders,
 and use with other agents)

IT Cell adhesion molecules
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (VCAM-1 (vascular cell adhesion mol. 1); cyclo(prolylglycine) for
 treatment of neural disorders, and use with other agents)

IT Encephalomyelitis
 (acute or chronic; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Cerebrospinal fluid
 (artificial; cyclo(prolylglycine) for treatment of neural disorders)

IT Neurotrophic factors
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (brain-derived; cyclo(prolylglycine) for treatment of neural disorders,
 and use with other agents)

IT Myelin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (central pontine myelinolysis; cyclo(prolylglycine) for treatment of
 neural disorders)

IT Brain
 (cerebellum, cerebellar neuron; cyclo(prolylglycine) for treatment of
 neural disorders)

IT Brain
 (cerebellum, damage; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Brain, disease
 (cerebellum, degeneration; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Brain
 (cerebellum, hemorrhage; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Brain
 (cerebellum, infarction; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Injury
 (cerebral; cyclo(prolylglycine) for treatment of neural disorders)

IT Surgery
 (coronary artery bypass; cyclo(prolylglycine) for treatment of neural
 disorders)

IT Artery

(coronary, bypass surgery; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(corpus striatum; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(cortex; cyclo(prolylglycine) for treatment of neural disorders)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic; cyclo(prolylglycine) for treatment of neural disorders)

IT Alzheimer's disease
Anti-Alzheimer's agents
Anti-ischemic agents
Antiparkinsonian agents
Apoptosis
Asphyxia
Drug delivery systems
Hypoxia
Ischemia
Motor skill disorders
Necrosis
Nerve
Nervous system, disease
Nervous system agents
Neurotoxicity
Parkinson's disease
Wernicke-Korsakoff syndrome
(cyclo(prolylglycine) for treatment of neural disorders)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cyclo(prolylglycine) for treatment of neural disorders)

IT Anti-inflammatory agents
Glutamate antagonists
(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Ciliary neurotrophic factor
Insulin-like growth factor-binding proteins
Interleukins
Leukemia inhibitory factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nerve, disease
(degeneration; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(dentate gyrus; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(diffuse cerebral sclerosis of Schilder; cyclo(prolylglycine) for treatment of neural disorders)

IT Drugs
(drug-induced cerebellar disorders; cyclo(prolylglycine) for treatment of neural disorders)

IT Endocrine system
(endocrine cerebellar disorders; cyclo(prolylglycine) for treatment of neural disorders)

IT Neurotrophic factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glial-derived; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Brain
(hippocampus, CA4; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(hippocampus, sector CA1; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain

(hippocampus, sector CA2; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain

(hippocampus, sector CA3; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hst/Kfgk gene product; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Drug delivery systems

(inhalants; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(injections, i.m.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(injections, i.p.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(injections, i.v.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(injections, s.c.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(injections; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease

(injury; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(int-2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Metabolism

(metabolic cerebellar disorders; cyclo(prolylglycine) for treatment of neural disorders)

IT Antibodies and Immunoglobulins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal, MECA-367; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nervous system, disease

(multiple system atrophy; cyclo(prolylglycine) for treatment of neural disorders)

IT Inflammation

Spinal cord, disease

(myelitis, transverse; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(nasal; cyclo(prolylglycine) for treatment of neural disorders)

IT Encephalitis

(necrotizing hemorrhagic; cyclo(prolylglycine) for treatment of neural disorders)

IT Nerve

(neural fasciculation; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease

(neuromyelitis optica; cyclo(prolylglycine) for treatment of neural disorders)

IT Cytoprotective agents

(neuroprotective; cyclo(prolylglycine) for treatment of neural disorders)

IT Inflammation

Nerve, disease

(optic neuritis; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems

(oral; cyclo(prolylglycine) for treatment of neural disorders)

IT Axon

(outgrowth; cyclo(prolylglycine) for treatment of neural disorders)

IT Gelatins, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical composition including; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease
 (progressive multifocal leukoencephalopathy; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
 (rectal; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (somatotropin-binding; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nervous system, disease
 (spinocerebellar ataxia 1; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia 6; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia, 2; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia, 4; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia, 5; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia, 7; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia, dominantly or recessively inherited; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
 (spinocerebellar ataxia, sporadic; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease
 (stroke; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease
 (trauma; cyclo(prolylglycine) for treatment of neural disorders)

IT Interferons
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (χ and consensus; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Interferons
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (α ; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α L; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α 4; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α 4 β 1; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Transforming growth factors
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (β 1-; cyclo(prolylglycine) for treatment of neural disorders, and

use with other agents)

IT Interferons
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (β; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (β7; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT 51-21-8, 5-Fluorouracil
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (5-fluorouracil-induced loss of Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)

IT 64-17-5, Ethanol, biological studies
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (alc. cerebellar degeneration; cyclo(prolylglycine) for treatment of neural disorders)

IT 56-40-6, Glycine, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (binding; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT 3705-27-9
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclo(prolylglycine) for treatment of neural disorders)

IT 492-27-3, Kynurenic acid 533-45-9, Clomethiazole 9002-72-6, Growth hormone 9061-61-4, Nerve growth factor 14611-51-9, Selegiline 50913-82-1, ORG 2766 67763-96-6, IGF-1 67763-97-7, IGF-2 77086-22-7, MK-801 80714-61-0, Semax 104987-11-3, FK506 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 106956-32-5, Oncostatin M 109836-81-9, L-threo-1-Phenyl-2-decanoylamino-3-morpholino-1-propanol 114949-22-3, Activin 118876-58-7, NBQX 123584-45-2, Fibroblast growth factor 4 130939-41-2, Fibroblast growth factor 6 130939-66-1, Neurotrophin 3 140698-57-3, Activity-dependent neurotrophic factor 143375-33-1, Neurotrophin 4 148348-14-5, Fibroblast growth factor 3 148348-15-6, Fibroblast growth factor 7 153436-22-7, GV 150526 161832-65-1, LY300164 161832-71-9, LY303070 171758-70-6, Fibroblast growth factor 10 **186495-99-8**, NPS 1506 204719-95-9, Fibroblast growth factor 16 524706-48-7, GV 1505260
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT 147-94-4, Cytosine arabinoside
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (cytosine arabinoside-induced loss of Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)

IT 69-65-8, Mannitol 9004-54-0, Dextran, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical composition including; cyclo(prolylglycine) for treatment of neural disorders)

IT 57-41-0, Phenytoin
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (phenytoin-induced cerebellar atrophy; cyclo(prolylglycine) for treatment of neural disorders)

L5 ANSWER 10 OF 27 USPATFULL on STN

ACCESSION NUMBER: 2003:283245 USPATFULL

TITLE: Anticonvulsant and central nervous system-depressing bis (fluorophenyl) alkylamides and their uses

INVENTOR(S): Balandrin, Manuel F., Sandy, UT, UNITED STATES
 VanWagenen, Bradford C., Salt Lake City, UT, UNITED STATES
 Artman, Linda D., Salt Lake City, UT, UNITED STATES
 Mueller, Alan L., Salt Lake City, UT, UNITED STATES
 Smith, Daryl, Salt Lake City, UT, UNITED STATES
 Moe, Scott T., Boston, MA, UNITED STATES

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc. (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2003199589 | A1 | 20031023 |
| APPLICATION INFO.: | US 2003-429060 | A1 | 20030502 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 2000-587179, filed on 2 Jun 2000, PENDING Continuation of Ser. No. WO 1998-US26315, filed on 9 Dec 1998, PENDING | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1997-69005P | 19971210 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | NPS PHARMACEUTICALS, INC. C/O FOLEY & LARDNER, P.O. BOX 80278, SAN DIEGO, CA, 92138-0278 | |
| NUMBER OF CLAIMS: | 30 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 4 Drawing Page(s) | |
| LINE COUNT: | 1342 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

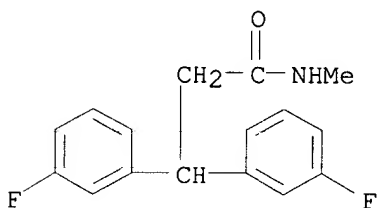
AB Bis(Fluorophenyl)alkylamides have been chemically synthesized which possess beneficial pharmacological properties (e.g., anticonvulsant activity) useful for the treatment of neurological diseases or disorders, such as, for example, epilepsy, convulsions, and seizure disorders. The preferred compounds of the invention also cause little sedation and have high therapeutic and protective indices in animal models of epilepsy. These compounds further possess long pharmacologic half-lives, which, in practical clinical therapeutic application, should translate into once-a-day dosing, of great benefit to patients suffering from these diseases and/or disorders. These compounds may also be of further clinical utility in the treatment of other diseases and disorders of the central and peripheral nervous systems, or diseases or disorders affected by them, including, but not limited to, spasticity, skeletal muscle spasms and pain, restless leg syndrome, anxiety and stress, and bipolar disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **200429-55-6P**
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

RN 200429-55-6 USPATFULL

CN Benzenepropanamide, 3-fluoro- β -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT Nervous system
 (Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system
 (amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Spinal cord
 (injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (manic bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

system agents)

IT Mental disorder
(mood-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Anti-Alzheimer's agents

IT Anticonvulsants

IT Antimigraine agents

IT Antiparkinsonian agents

IT Anxiolytics

IT Nervous system agents
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Brain, disease
(stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Head
(trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Multiple sclerosis
(treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P 200429-53-4P
200429-54-5P **200429-55-6P** 227289-95-4P 227290-02-0P
227290-09-7P 227290-12-2P 227290-22-4P 227290-28-0P 227290-37-1P
227290-41-7P 227290-47-3P 227290-50-8P 227290-56-4P
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions
124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,
4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,
Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,
Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate
3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P
50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P
170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P
227290-64-4P
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

L5 ANSWER 11 OF 27 USPATFULL on STN
ACCESSION NUMBER: 2003:159916 USPATFULL
TITLE: Therapeutic agent composition and method of use
INVENTOR(S): Tran, Loi H., Elk Grove, CA, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2003109531 | A1 | 20030612 |
| APPLICATION INFO.: | US 2002-292732 | A1 | 20021112 (10) |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | NZ 2001-515432 | 20011113 |
| | US 2002-405909P | 20020826 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DAVID R PRESTON & ASSOCIATES, 12625 HIGH BLUFF DRIVE, SUITE 205, SAN DIEGO, CA, 92130
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1144

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the use of cyclic Prolyl Glycine ("cyclic PG" or "cPG") and analogs and mimetics thereof, as neuroprotective agents for the treatment and or prevention of neurological disorders including

but not limited to cerebral ischemia or cerebral infarction resulting from a range of phenomena, such as thromboembolic or hemorrhagic stroke, cerebral basospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia such as from drowning, pulmonary surgery, and cerebral trauma, as well as to the treatment and prevention of chronic neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, and Huntington's disease, and as anticonvulsants.

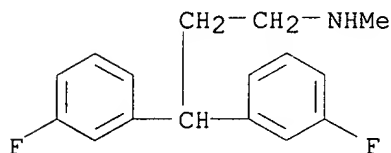
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186495-99-8, NPS 1506

(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

RN 186495-99-8 USPATFULL

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Bone morphogenetic proteins

(2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Glutamate receptors

(AMPA-binding, antagonists; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Growth factors, animal

(Androgen-induced growth factor; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Brain, disease

IT Nervous system, disease

(Devic's disease; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins

(FHF-1; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Proteins

(FHF-2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Proteins

(FHF-3; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Proteins

(FHF-4; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Growth factors, animal

(Glial-activating factor; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nervous system, disease

(Huntington's chorea; cyclo(prolylglycine) for treatment of neural disorders)

IT Cell adhesion molecules

(ICAM (intercellular adhesion mol.); cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins

(LPAM-1 (lymphocyte Peyer's patch high endothelial venule adhesion mol. 1); cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Cell adhesion molecules

(MAdCAM-1 (mucosal addressin cell adhesion mol.-1);

cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nervous system, disease
(Machado-Joseph; cyclo(prolylglycine) for treatment of neural disorders)

IT Nerve
(Purkinje cell, 5-fluorouracil- or cytosine arabinoside-induced loss of Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)

IT Tumor necrosis factors
(TNF- α ; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Cell adhesion molecules
(VCAM-1; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Encephalomyelitis
(acute or chronic; cyclo(prolylglycine) for treatment of neural disorders)

IT Integrins
(antigens CD11a; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Cerebrospinal fluid
(artificial; cyclo(prolylglycine) for treatment of neural disorders)

IT Neurotrophic factors
(brain-derived; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Myelin
(central pontine myelinolysis; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(cerebellum, cerebellar neuron; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(cerebellum, damage; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease
(cerebellum, degeneration; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(cerebellum, hemorrhage; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(cerebellum, infarction; cyclo(prolylglycine) for treatment of neural disorders)

IT Artery
(coronary, bypass surgery; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(corpus striatum; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(cortex; cyclo(prolylglycine) for treatment of neural disorders)

IT Peptides, biological studies
(cyclic; cyclo(prolylglycine) for treatment of neural disorders)

IT Alzheimer's disease

IT Anti-Alzheimer's agents

IT Anti-ischemic agents

IT Antiparkinsonian agents

IT Apoptosis

IT Asphyxia

IT Drug delivery systems

IT Hypoxia, animal

IT Ischemia

IT Necrosis

IT Nervous system, disease

IT Nervous system agents

IT Parkinson's disease

IT Wernicke-Korsakoff syndrome
(cyclo(prolylglycine) for treatment of neural disorders)

IT Toxins

(cyclo(prolylglycine) for treatment of neural disorders)

IT Anti-inflammatory agents

IT Glutamate antagonists
(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Ciliary neurotrophic factor

IT Insulin-like growth factor-binding proteins

IT Interleukins

IT Leukemia inhibitory factor
(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nerve, disease
(degeneration; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(dentate gyrus; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(diffuse cerebral sclerosis of Schilder; cyclo(prolylglycine) for treatment of neural disorders)

IT Drugs
(drug-induced cerebellar disorders; cyclo(prolylglycine) for treatment of neural disorders)

IT Endocrine system
(endocrine cerebellar disorders; cyclo(prolylglycine) for treatment of neural disorders)

IT Neurotrophic factors
(glial-derived; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Brain
(hippocampus, CA4; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(hippocampus, sector CA1; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(hippocampus, sector CA2; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain
(hippocampus, sector CA3; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins
(hst/Kfgk gene product; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Drug delivery systems
(inhalants; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(injections, i.m.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(injections, i.p.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(injections, i.v.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(injections, s.c.; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(injections; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease
(injury; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins
(int-2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT CD antigens

IT Integrins
(integrin $\beta 7$; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Metabolism
(metabolic cerebellar disorders; cyclo(prolylglycine) for treatment of

neural disorders)

IT Antibodies
(monoclonal, MECA-367; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Behavior
(motor, disorder; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(multiple system atrophy; cyclo(prolylglycine) for treatment of neural disorders)

IT Spinal cord, disease
(myelitis, transverse; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(nasal; cyclo(prolylglycine) for treatment of neural disorders)

IT Encephalitis
(necrotizing hemorrhagic; cyclo(prolylglycine) for treatment of neural disorders)

IT Nerve
(neural fasciculation; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(neuromyelitis optica; cyclo(prolylglycine) for treatment of neural disorders)

IT Cytoprotective agents
(neuroprotectants; cyclo(prolylglycine) for treatment of neural disorders)

IT Toxicity
(neurotoxicity; cyclo(prolylglycine) for treatment of neural disorders)

IT Nerve, disease
(optic, neuritis; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(oral; cyclo(prolylglycine) for treatment of neural disorders)

IT Axon
(outgrowth; cyclo(prolylglycine) for treatment of neural disorders)

IT Gelatins, biological studies
(pharmaceutical composition including; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease
(progressive multifocal leukoencephalopathy; cyclo(prolylglycine) for treatment of neural disorders)

IT Drug delivery systems
(rectal; cyclo(prolylglycine) for treatment of neural disorders)

IT Proteins
(somatotropin-binding; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Nervous system, disease
(spinocerebellar ataxia 1; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(spinocerebellar ataxia 6; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(spinocerebellar ataxia, 2; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(spinocerebellar ataxia, 4; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(spinocerebellar ataxia, 5; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(spinocerebellar ataxia, 7; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease
(spinocerebellar ataxia, dominantly or recessively inherited; cyclo(prolylglycine) for treatment of neural disorders)

IT Nervous system, disease

(spinocerebellar ataxia, sporadic; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease

(stroke; cyclo(prolylglycine) for treatment of neural disorders)

IT Nerve

(toxicity; cyclo(prolylglycine) for treatment of neural disorders)

IT Brain, disease

(trauma; cyclo(prolylglycine) for treatment of neural disorders)

IT Interferons

(χ and consensus; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Interferons

(α ; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins

($\alpha 4$; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins

($\alpha 4 \beta 1$; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Transforming growth factors

($\beta 1$ -; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Interferons

(β ; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT Integrins

($\beta 2$; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT 51-21-8, 5-Fluorouracil

(5-fluorouracil-induced loss of Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)

IT 64-17-5, Ethanol, biological studies

(alc. cerebellar degeneration; cyclo(prolylglycine) for treatment of neural disorders)

IT 56-40-6, Glycine, biological studies

(binding; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT 3705-27-9

(cyclo(prolylglycine) for treatment of neural disorders)

IT 492-27-3, Kynurenic acid 533-45-9, Clomethiazole 9002-72-6, Growth

hormone 9061-61-4, Nerve growth factor 14611-51-9, Selegiline

50913-82-1, ORG 2766 67763-96-6, IGF-1 67763-97-7, IGF-2

77086-22-7, MK-801 80714-61-0, Semax 104987-11-3, FK506

106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic

fibroblast growth factor 106956-32-5, Oncostatin M 109836-81-9,

L-threo-1-Phenyl-2-decanoylamino-3-morpholino-1-propanol 114949-22-3,

Activin 118876-58-7, NBQX 123584-45-2, Fibroblast growth factor 4

130939-41-2, Fibroblast growth factor 6 130939-66-1, Neurotrophin 3

140698-57-3, Activity-dependent neurotrophic factor 143375-33-1,

Neurotrophin 4 148348-14-5, Fibroblast growth factor 3 148348-15-6,

Fibroblast growth factor 7 153436-38-5, GV150526 161832-65-1,

LY300164 161832-71-9, LY303070 171758-70-6, Fibroblast growth factor

10 **186495-99-8**, NPS 1506 204719-95-9, Fibroblast growth

factor 16 524706-48-7, GV 1505260

(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

IT 147-94-4, Cytosine arabinoside

(cytosine arabinoside-induced loss of Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)

IT 87-78-5, Mannitol 9004-54-0, Dextran, biological studies

(pharmaceutical composition including; cyclo(prolylglycine) for treatment of neural disorders)

IT 57-41-0, Phenytoin

(phenytoin-induced cerebellar atrophy; cyclo(prolylglycine) for treatment of neural disorders)

TITLE: Anticonvulsant and central nervous system-depressing
bis(fluorophenyl)alkylamides and their uses

INVENTOR(S): Balandrin, Manuel F., Sandy, UT, United States
VanWagenen, Bradford C., Salt Lake City, UT, United States
Artman, Linda D., Salt Lake City, UT, United States
Mueller, Alan L., Salt Lake City, UT, United States
Smith, Daryl, Salt Lake City, UT, United States
Moe, Scott T., Salt Lake City, UT, United States

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., Salt Lake City, UT, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6617358 | B1 | 20030909 |
| APPLICATION INFO.: | US 2000-587179 | | 20000602 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. WO 1998-US26315, filed on 9 Dec 1998 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1997-69005P | 19971210 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Kumar, Shailendra | |
| NUMBER OF CLAIMS: | 19 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 9 Drawing Figure(s); 8 Drawing Page(s) | |
| LINE COUNT: | 1387 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Bis(Fluorophenyl)alkylamides have been chemically synthesized which possess beneficial pharmacological properties (e.g., anticonvulsant activity) useful for the treatment of neurological diseases or disorders, such as, for example, epilepsy, convulsions, and seizure disorders. The preferred compounds of the invention also cause little sedation and have high therapeutic and protective indices in animal models of epilepsy. These compounds further possess long pharmacological half-lives, which, in practical clinical therapeutic application, should translate into once-a-day dosing, of great benefit to patients suffering from these diseases and/or disorders. These compounds may also be of further clinical utility in the treatment of other diseases and disorders of the central and peripheral nervous systems, or diseases or disorders affected by them, including, but not limited to, spasticity, skeletal muscle spasms and pain, restless leg syndrome, anxiety and stress, and bipolar disorder.

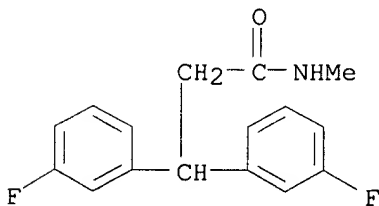
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **200429-55-6P**

(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

RN 200429-55-6 USPATFULL

CN Benzenepropanamide, 3-fluoro-β-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT Nervous system

(Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system

(amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

- IT Spinal cord
(injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT Mental disorder
(manic bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT Mental disorder
(mood-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT Anti-Alzheimer's agents
- IT Anticonvulsants
- IT Antimigraine agents
- IT Antiparkinsonian agents
- IT Anxiolytics
- IT Nervous system agents
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT Brain, disease
(stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT Head
(trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT Multiple sclerosis
(treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P 200429-53-4P
200429-54-5P **200429-55-6P** 227289-95-4P 227290-02-0P
227290-09-7P 227290-12-2P 227290-22-4P 227290-28-0P 227290-37-1P
227290-41-7P 227290-47-3P 227290-50-8P 227290-56-4P
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions
124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,
4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,
Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,
Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate
3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)
- IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P
50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P
170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P
227290-64-4P
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

L5 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:924889 CAPLUS

DOCUMENT NUMBER: 140:317215

TITLE: Synthesis and brain regional distribution of [11C]NPS
1506 in mice and rat: An N-methyl-D-aspartate (NMDA)
receptor antagonist

AUTHOR(S): Fuchigami, Takeshi; Haradahira, Terushi; Arai, Takuya;
Okauchi, Takashi; Maeda, Jun; Suzuki, Kazutoshi;
Yamamoto, Fumihiko; Suhara, Tetsuya; Sasaki, Shigeki;
Maeda, Minoru

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyushu
University, Fukuoka, 812-8582, Japan

SOURCE: Biological & Pharmaceutical Bulletin (2003), 26(11),
1570-1573

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

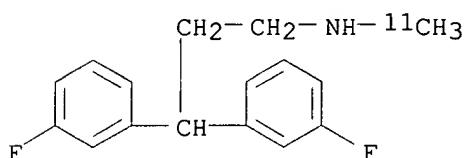
LANGUAGE: English

AB NPS 1506 [3-fluoro- γ -(3-fluorophenyl)-N-methylbenzenepropamine] is representative of a non-psychotomimetic class of N-methyl-D-aspartate (NMDA) receptor antagonists. [11C]NPS 1506 was prepared at high radiochem. purity (>98%) with a specific activity of around 50 GBq/ μ mol at the end of synthesis by methylation of the desmethyl precursor with [11C]methyl iodide in the presence of NaH. Biodistribution of [11C]NPS 1506 in mice and rat demonstrated that uptake into the brain was rapid and occurred at high levels. [11C]NPS 1506 showed no appreciable specific binding in rodent brains under in vivo conditions, possibly because of both a large non-specific bound fraction and low in vitro binding affinity for NMDA receptors.

IT **677764-00-0P**
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

RN 677764-00-0 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-(methyl-11C)-, hydrochloride (9CI) (CA INDEX NAME)

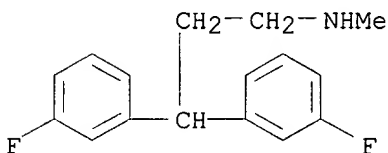


● HCl

IT **186495-99-8P**, NPS 1506
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists
(NMDA antagonists; NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT Blood-brain barrier
Brain
Isotope indicators
(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NMDA-binding; NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT **677764-00-0P**

RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT 186495-99-8P, NPS 1506

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT 542-92-7, Cyclopentadiene, reactions 170019-10-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT 677763-98-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:777693 CAPLUS

DOCUMENT NUMBER: 137:299911

TITLE: Neuroprotectant formulations

INVENTOR(S): Hesson, David P.; Frazer, Glenn D.; Ross, Douglas

PATENT ASSIGNEE(S): Neuron Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2002078670 | A1 | 20021010 | WO 2002-US5885 | 20020228 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| EP 1370240 | A1 | 20031217 | EP 2002-733809 | 20020228 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| US 2002193285 | A1 | 20021219 | US 2002-90441 | 20020304 |
| PRIORITY APPLN. INFO.: | | | US 2001-331360P | P 20010302 |
| | | | US 2001-798880 | A 20010302 |
| | | | WO 2002-US5885 | W 20020228 |

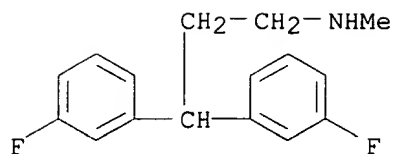
AB A method of treating an animal that has suffered damage to cerebrospinal tissue or that has an indication creating a risk of damage to cerebrospinal tissue, comprises injecting a physiologically acceptable cerebrospinal perfusion fluid into a first catheter into the cerebrospinal pathway. The cerebrospinal perfusion fluid has a neuroprotecting effective amount of a neuroprotectant, withdrawing fluid at a second catheter into the cerebrospinal pathway to create a flow and flow pathway between the first and second catheters and c. maintaining the flow for a period of time adapted to perfuse an affected tissue.

IT 186495-99-8, NPS 1506

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (neuroprotectant formulations)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Medical goods
(catheters; neuroprotectant formulations)

IT Nervous system, disease
(degeneration; neuroprotectant formulations)

IT Alzheimer's disease
Anti-inflammatory agents
Cerebrospinal fluid
Drug delivery systems
Human
Multiple sclerosis
Perfusion
(neuroprotectant formulations)

IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotectant formulations)

IT Cytoprotective agents
(neuroprotective; neuroprotectant formulations)

IT Anti-inflammatory agents
(nonsteroidal; neuroprotectant formulations)

IT Brain, disease
(stroke; neuroprotectant formulations)

IT Injury
(trauma; neuroprotectant formulations)

IT 169592-56-7, Caspase 3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; neuroprotectant formulations)

IT 50-81-7, Ascorbic acid, biological studies 51-55-8, Atropine, biological studies 533-45-9, Clomethiazole 987-78-0, Citicoline 2149-70-4, Nitroarginine 2156-56-1, Ceresine 6735-59-7, Pralidoxime 19982-08-2, Memantine 22059-21-8 22503-72-6 23052-81-5 23210-56-2, Ifenprodil 31409-32-2, MDL 27192 55985-32-5, Nicardipine 66085-59-4, Nimodipine 72784-43-1, ACPM 72784-47-5, ACPCE 77086-21-6, Dizocilpine 79055-68-8 88191-84-8, MDL 28170 107452-89-1, Ziconotide 110347-85-8, Selfotel 111900-32-4 112924-45-5, Sinnabidiol 119431-25-3, Eliprodil 123931-04-4 125546-04-5 128073-45-0 128298-28-2, Remacemide 130931-65-6 137160-11-3, Cerestat 142852-51-5, TAK 147 144665-07-6, Lubeluzole 153504-81-5, Licostinel 158798-83-5, AK 275 160399-35-9, AK 295 168021-79-2, NXY 059 173952-44-8, SYM 2206 175615-45-9, LY 287041 185243-69-0, Etanercept **186495-99-8**, NPS 1506 223723-79-3, AEOL 10113 286475-30-7, AEOL 10150 466685-97-2 466685-98-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotectant formulations)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 27 USPATFULL on STN

ACCESSION NUMBER: 2002:337920 USPATFULL

TITLE: Neuroprotectants formulations and methods

INVENTOR(S): Hesson, David P., Malvern, PA, UNITED STATES
Frazer, Glen D., Wynnewood, PA, UNITED STATES
Ross, Douglas, North wales, PA, UNITED STATES

| | NUMBER | KIND | DATE |
|---------------------|---------------|------|----------|
| PATENT INFORMATION: | US 2002193285 | A1 | 20021219 |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2001-331360P | 20010302 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | ALLEN BLOOM, C/O DECHERT, PRINCETON PIKE CORPORATION CENTER, P.O. BOX 5218, PRINCETON, NJ, 08543-5218 | |
| NUMBER OF CLAIMS: | 16 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 1 Drawing Page(s) | |
| LINE COUNT: | 870 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided is a method of treating in an animal that has suffered damage to cerebrospinal tissue or that has an indication creating a risk of damage to cerebrospinal tissue, the method comprising: a. injecting a physiologically acceptable cerebrospinal perfusion fluid into a first catheter into the cerebrospinal pathway, which cerebrospinal perfusion fluid has a neuroprotecting effective amount of a neuroprotectant; b. withdrawing fluid at a second catheter into the cerebrospinal pathway to create a flow and flow pathway between the first and second catheters; and c. maintaining the flow for a period of time adapted to perfuse an affected tissue.

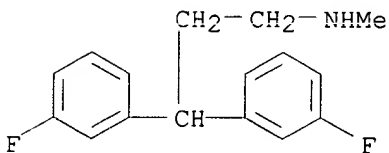
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186495-99-8, NPS 1506

(neuroprotectant formulations)

RN 186495-99-8 USPTAFULL

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Medical goods
(catheters; neuroprotectant formulations)

IT Nervous system
(degeneration; neuroprotectant formulations)

IT Alzheimer's disease

IT Anti-inflammatory agents

IT Cerebrospinal fluid

IT Drug delivery systems

IT Human

IT Multiple sclerosis

IT Perfusion
(neuroprotectant formulations)

IT Albumins, biological studies
(neuroprotectant formulations)

IT Cytoprotective agents
(neuroprotectants; neuroprotectant formulations)

IT Anti-inflammatory agents
(nonsteroidal; neuroprotectant formulations)

IT Brain, disease
(stroke; neuroprotectant formulations)

IT Injury
(trauma; neuroprotectant formulations)

IT 169592-56-7, Caspase 3
(inhibitor; neuroprotectant formulations)

IT 50-81-7, Ascorbic acid, biological studies 51-55-8, Atropine,
biological studies 533-45-9, Clomethiazole 987-78-0, Citicoline
2149-70-4, Nitroarginine 2156-56-1, Ceresine 6735-59-7, Pralidoxime
19982-08-2, Memantine 22059-21-8 22503-72-6 23052-81-5
23210-56-2, Ifenprodil 31409-32-2, MDL 27192 55985-32-5, Nicardipine
66085-59-4, Nimodipine 72784-43-1, ACPCM 72784-47-5, ACPCE
77086-21-6, Dizocilpine 79055-68-8 88191-84-8, MDL 28170
107452-89-1, Ziconotide 110347-85-8, Selfotel 111900-32-4
112924-45-5, Sinnabidiol 119431-25-3, Eliprodil 123931-04-4
125546-04-5 128073-45-0 128298-28-2, Remacemide 130931-65-6
137160-11-3, Cerestat 142852-51-5, TAK 147 144665-07-6, Lubeluzole
153504-81-5, Licostinel 158798-83-5, AK 275 160399-35-9, AK 295
168021-79-2, NXY 059 173952-44-8, SYM 2206 175615-45-9, LY 287041
185243-69-0, Etanercept **186495-99-8**, NPS 1506 223723-79-3,
AEOL 10113 286475-30-7, AEOL 10150 466685-97-2 466685-98-3
(neuroprotectant formulations)

L5 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2000:381465 CAPLUS

DOCUMENT NUMBER: 133:30571

TITLE: Preparation of aralkylamines active at
receptor-operated calcium channels as neuroprotectants

INVENTOR(S): Mueller, Alan L.; Balandrin, Manuel F.; Vanwagenen,
Bradford C.; Delmar, Eric G.; Moe, Scott T.; Artman,
Linda D.; Barmore, Robert M.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: U.S., 133 pp., Cont.-in-part of WO 9511663.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|--|----------|-----------------|----------|
| US 6071970 | A | 20000606 | US 1995-485038 | 19950607 |
| CA 2182680 | AA | 19950817 | CA 1994-2182680 | 19941026 |
| WO 9521612 | A2 | 19950817 | WO 1994-US12293 | 19941026 |
| WO 9521612 | A3 | 19950921 | | |
| W: | AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US | | | |
| RW: | KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| CN 1148337 | A | 19970423 | CN 1994-195074 | 19941026 |
| CN 1088585 | B | 20020807 | | |
| ES 2156162 | T3 | 20010616 | ES 1994-932057 | 19941026 |
| EP 1123922 | A2 | 20010816 | EP 2000-121960 | 19941026 |
| EP 1123922 | A3 | 20040102 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | |
| PT 743853 | T | 20011031 | PT 1994-932057 | 19941026 |
| CA 2223978 | AA | 19961219 | CA 1996-2223978 | 19960607 |
| WO 9640097 | A1 | 19961219 | WO 1996-US10201 | 19960607 |
| W: | AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | |
| RW: | AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | |
| AU 9661125 | A1 | 19961230 | AU 1996-61125 | 19960607 |
| AU 716122 | B2 | 20000217 | | |
| EP 831799 | A1 | 19980401 | EP 1996-918477 | 19960607 |
| EP 831799 | B1 | 20030502 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| CN 1192679 | A | 19980909 | CN 1996-196042 | 19960607 |
| JP 11506469 | T2 | 19990608 | JP 1996-502238 | 19960607 |
| BR 9609019 | A | 19990706 | BR 1996-9019 | 19960607 |
| NZ 310344 | A | 20010330 | NZ 1996-310344 | 19960607 |

| | | | | |
|---------------|----|----------|----------------|----------|
| AT 238782 | E | 20030515 | AT 1996-918477 | 19960607 |
| PL 185492 | B1 | 20030530 | PL 1996-323871 | 19960607 |
| PT 831799 | T | 20030930 | PT 1996-918477 | 19960607 |
| ES 2197945 | T3 | 20040116 | ES 1996-918477 | 19960607 |
| RU 2246300 | C2 | 20050220 | RU 1998-100454 | 19960607 |
| US 6017965 | A | 20000125 | US 1996-763480 | 19961211 |
| HK 1008980 | A1 | 20031107 | HK 1998-109748 | 19980806 |
| US 6211245 | B1 | 20010403 | US 1998-186341 | 19981104 |
| US 6051610 | A | 20000418 | US 1999-252433 | 19990218 |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| US 2002004522 | A1 | 20020110 | US 2001-825373 | 20010402 |
| US 6750244 | B2 | 20040615 | | |
| JP 2004002437 | A2 | 20040108 | JP 2003-158350 | 20030603 |
| US 2004171670 | A1 | 20040902 | US 2004-797355 | 20040309 |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|----|----------|
| US 1993-14813 | B2 | 19930208 |
| US 1994-194210 | B2 | 19940208 |
| US 1994-288668 | B2 | 19940809 |
| WO 1994-US12293 | A2 | 19941026 |
| US 1994-288688 | A2 | 19940811 |
| EP 1994-932057 | A3 | 19941026 |
| JP 1995-521191 | A3 | 19941026 |
| US 1995-485038 | A | 19950607 |
| US 1996-663013 | A2 | 19960607 |
| WO 1996-US10201 | W | 19960607 |
| AU 1997-13525 | A3 | 19961211 |
| US 1996-763480 | A2 | 19961211 |
| US 1997-869154 | B2 | 19970604 |
| US 1997-873011 | A1 | 19970611 |
| US 1998-186341 | A1 | 19981104 |
| US 2001-825373 | A1 | 20010402 |

OTHER SOURCE(S): MARPAT 133:30571

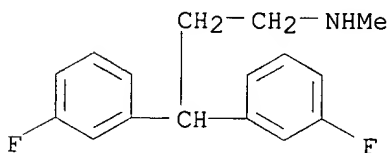
AB Title compds., e.g., RCHR4CR1R5CR2R6R7 [R = (un)substituted Ph; R1,R5 = H, OH, (hydroxy)alkyl, alkoxy, acyloxy; R2,R6 = H or hydroxyalkyl; R1R2 = (CH2)n or (CH2)nNR3; R3 = H, alkyl, CH2CH2OH; R4 = (cyclo)alkyl, or (un)substituted Ph; R7 = N(R3)2; R7 = H when R1R2 = (CH2)nNR3; n = 1-6] were prepared. Thus, (4-FC6H4)2CO was condensed with (EtO)2P(O)CH2CN and the product converted in 2 reduction steps to (4-FC6H4)2CHCH2CH2NH2. Data for biol. activity of title compds. were given.

IT **186495-49-8P 186495-56-7P 186495-99-8P 273409-53-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

RN 186495-49-8 CAPLUS

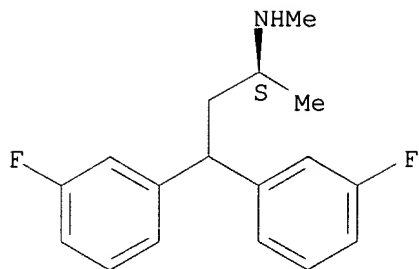
CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



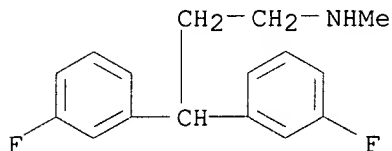
RN 186495-56-7 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,α-dimethyl-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

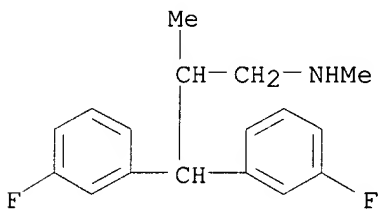


RN 186495-99-8 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
 hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 273409-53-3 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,β-dimethyl-
 (9CI) (CA INDEX NAME)



IT Ionophores
 (NMDA receptor complex; preparation of aralkylamines active at
 receptor-operated calcium channels as neuroprotectants)

IT Glutamate receptors
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
 (Biological study)
 (NMDA-binding, ionophore complex; preparation of aralkylamines active at
 receptor-operated calcium channels as neuroprotectants)

IT Nervous system
 (degeneration, treatment; preparation of aralkylamines active at
 receptor-operated calcium channels as neuroprotectants)

IT Cytoprotective agents
 (neuroprotectants; preparation of aralkylamines active at receptor-operated
 calcium channels as neuroprotectants)

IT Calcium channel
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (preparation of aralkylamines active at receptor-operated calcium channels
 as neuroprotectants)

IT 5586-73-2P 28075-29-8P 90531-05-8P 133805-32-0P 144451-98-9P
 144452-04-0P 144576-90-9P 148920-48-3P 170018-48-1P 170018-49-2P
 170018-50-5P 170018-51-6P 170018-52-7P 170018-54-9P 170018-55-0P
 170018-56-1P 170018-57-2P 170018-63-0P 170018-66-3P 170018-67-4P
 170018-68-5P 170018-71-0P 170018-72-1P 170018-73-2P 170018-74-3P
 170018-75-4P 170018-76-5P 170018-77-6P 170018-78-7P 170018-79-8P

| | | | | |
|---------------------|---------------------|--------------|---------------------|--------------|
| 170018-80-1P | 170018-81-2P | 170018-82-3P | 170018-83-4P | 170018-84-5P |
| 170018-85-6P | 170018-86-7P | 170019-10-0P | 186495-37-4P | 186495-38-5P |
| 186495-39-6P | 186495-40-9P | 186495-41-0P | 186495-43-2P | 186495-44-3P |
| 186495-45-4P | 186495-46-5P | 186495-47-6P | 186495-48-7P | |
| 186495-49-8P | 186495-50-1P | 186495-51-2P | 186495-53-4P | |
| 186495-54-5P | 186495-56-7P | 186495-93-2P | 186495-94-3P | |
| 186495-95-4P | 186495-97-6P | 186495-98-7P | 186495-99-8P | |
| 186496-00-4P | 186496-02-6P | 186496-03-7P | 200430-18-8P | 217658-89-4P |
| 217658-94-1P | 217658-96-3P | 217659-01-3P | 217659-23-9P | 217660-61-2P |
| 273409-48-6P | 273409-49-7P | 273409-50-0P | 273409-51-1P | 273409-52-2P |

273409-53-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 62-23-7, p-Nitrobenzoic acid 85-41-6, Phthalimide 100-52-7, Benzaldehyde, reactions 105-34-0, Methyl cyanoacetate 107-13-1, 2-Propenenitrile, reactions 109-76-2, 1,3-Diaminopropane 110-60-1, 1,4-Diaminobutane 135-02-4, o-Anisaldehyde 285-67-6, Cyclopentene oxide 345-70-0, 3,3'-Difluorobenzophenone 443-73-2, 5-Fluoroindole-3-acetic acid 452-08-4, 2-Bromo-4-fluoroanisole 456-48-4, 3-Fluorobenzaldehyde 462-94-2, 1,5-Diaminopentane 529-20-4, 2-Methylbenzaldehyde 546-68-9 578-57-4, 2-Bromoanisole 587-04-2, 3-Chlorobenzaldehyde 932-31-0, 2-Methylphenylmagnesium bromide 1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1 5003-71-4 5460-29-7, N-(3-Bromopropyl)phthalimide 7300-34-7, 4,9-Dioxa-1,12-dodecandiamine 17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2, (S)-N-Benzyl- α -methylbenzylamine 50715-13-4 65416-24-2, Benzyl crotonate 77532-79-7, 5-Fluoro-2-methylbenzonitrile 122630-41-5 147624-13-3, 3-Fluoro-2-methylbenzaldehyde 168080-76-0, 3-Fluoro-2-methylbenzoyl chloride 263355-05-1, 3-Fluoro-2-methylphenylmagnesium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 455-67-4P 701-38-2P 4748-73-6P 14209-32-6P 35513-93-0P
38158-77-9P 51644-96-3P 75762-57-1P 83948-53-2P 98586-06-2P
101187-29-5P 114459-62-0P 122248-82-2P 122631-98-5P 122632-01-3P
122632-02-4P 128550-02-7P 128550-03-8P 128550-05-0P 128550-06-1P
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170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P 170019-19-9P
170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P 170019-24-6P
170019-25-7P 186496-31-1P 186496-32-2P 186496-33-3P 186496-34-4P
186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P
186496-40-2P 186496-41-3P 186496-42-4P 186496-44-6P 186496-45-7P
186496-46-8P 186496-48-0P 186496-51-5P 186496-52-6P 186496-53-7P
273409-54-4P 273409-55-5P 273409-56-6P 273409-57-7P 273409-58-8P
273409-62-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2000:66753 CAPLUS

DOCUMENT NUMBER: 132:107773

TITLE: Preparation of aralkylamines as NMDA receptor-ionophore complex antagonists

INVENTOR(S): Mueller, Alan L.; Balandrin, Manuel F.; Vanwagenen, Bradford C.; Moe, Scott T.; Delmar, Eric G.; Artman, Linda D.; Barmore, Robert M.; Smith, Daryl L.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: U.S., 112 pp., Cont.-in-part of U.S. Ser. No. 663.013.
CODEN: USXXAM

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 6
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 6017965 | A | 20000125 | US 1996-763480 | 19961211 |
| CA 2182680 | AA | 19950817 | CA 1994-2182680 | 19941026 |
| WO 9521612 | A2 | 19950817 | WO 1994-US12293 | 19941026 |
| WO 9521612 | A3 | 19950921 | | |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CN 1148337 | A | 19970423 | CN 1994-195074 | 19941026 |
| CN 1088585 | B | 20020807 | | |
| ES 2156162 | T3 | 20010616 | ES 1994-932057 | 19941026 |
| EP 1123922 | A2 | 20010816 | EP 2000-121960 | 19941026 |
| EP 1123922 | A3 | 20040102 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| PT 743853 | T | 20011031 | PT 1994-932057 | 19941026 |
| US 6071970 | A | 20000606 | US 1995-485038 | 19950607 |
| CA 2257234 | AA | 19971211 | CA 1996-2257234 | 19961211 |
| US 6211245 | B1 | 20010403 | US 1998-186341 | 19981104 |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| US 2002004522 | A1 | 20020110 | US 2001-825373 | 20010402 |
| US 6750244 | B2 | 20040615 | | |
| JP 2004002437 | A2 | 20040108 | JP 2003-158350 | 20030603 |
| US 2004171670 | A1 | 20040902 | US 2004-797355 | 20040309 |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|----|----------|
| US 1993-14813 | B2 | 19930208 |
| US 1994-194210 | B2 | 19940208 |
| US 1994-288668 | B2 | 19940809 |
| WO 1994-US12293 | A2 | 19941026 |
| US 1995-485038 | A2 | 19950607 |
| US 1996-663013 | A2 | 19960607 |
| US 1994-288688 | A2 | 19940811 |
| EP 1994-932057 | A3 | 19941026 |
| JP 1995-521191 | A3 | 19941026 |
| WO 1996-US19525 | A | 19961206 |
| AU 1997-13525 | A3 | 19961211 |
| US 1996-763480 | A2 | 19961211 |
| US 1997-869154 | B2 | 19970604 |
| US 1997-873011 | A1 | 19970611 |
| US 1998-186341 | A1 | 19981104 |
| US 2001-825373 | A1 | 20010402 |

OTHER SOURCE(S): MARPAT 132:107773

AB R7CHR4CR1R5CRR2R6[I; R = H or N(R3)2; R1,R5 = (un)substituted Ph, -CH2Ph, -OPh; R2,R6 = H or (hydroxy)alkyl; R1R2 = (CH2)n or (CH2)nNR3(CH2)n; R2R6 = NH; R3 = H, alkyl, CH2CH2OH, alkylphenyl; R4 = (un)substituted Ph, -pyridyl, -thienyl, etc.; R7 = (un)substituted Ph; n = 0-6] were prepared Thus, (3-FC6H4)2CO was condensed with (EtO)2P(O)CH2CO2Et and the product converted in 6 steps to (3-FC6H4)2CHCH2CHMeNH2. Data for biol. activity of I were given.

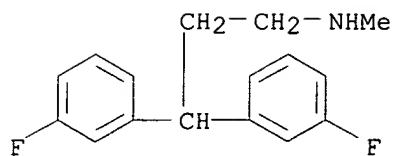
IT 186495-49-8P 186495-55-6P 186495-56-7P
 186495-99-8P 200429-55-6P 200429-70-5P
 200429-72-7P 200430-06-4P 200430-16-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

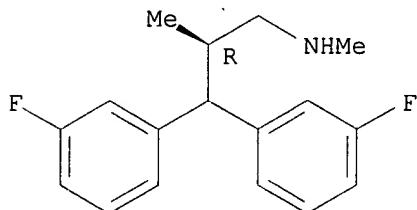
RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



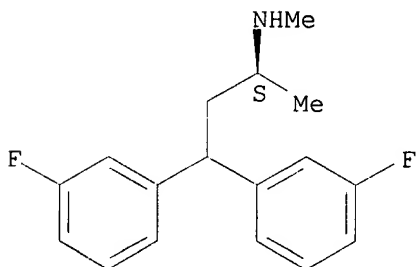
RN 186495-55-6 CAPLUS
 CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-,
 (β R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

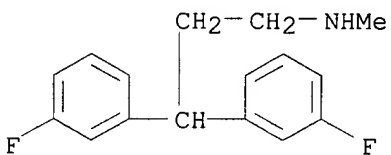


RN 186495-56-7 CAPLUS
 CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-,
 (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

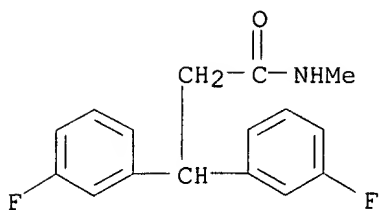


RN 186495-99-8 CAPLUS
 CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,
 hydrochloride (9CI) (CA INDEX NAME)



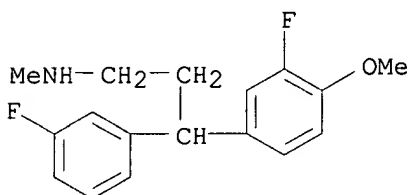
● HCl

RN 200429-55-6 CAPLUS
 CN Benzenepropanamide, 3-fluoro- β -(3-fluorophenyl)-N-methyl- (9CI) (CA
 INDEX NAME)



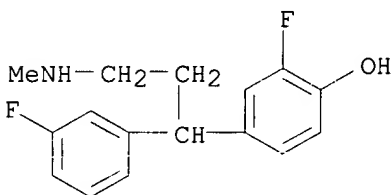
RN 200429-70-5 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-
(9CI) (CA INDEX NAME)



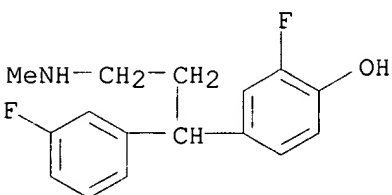
RN 200429-72-7 CAPLUS

CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]- (9CI) (CA
INDEX NAME)



RN 200430-06-4 CAPLUS

CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

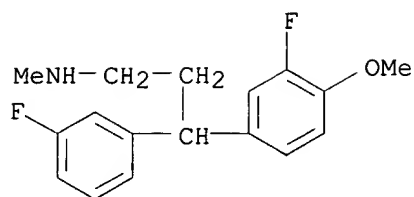
RN 200430-16-6 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-,
(2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 200429-70-5

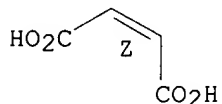
CMF C17 H19 F2 N O



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



IT Calcium channel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NMDA-binding glutamate receptor complex, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NMDA-binding, calcium channel complexes, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Nervous system
(disease, treatment; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(methyl-D-aspartate-binding, calcium channel complexes, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Cytoprotective agents
(neuroprotectants; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Analgesics
Anticonvulsants
(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 5586-73-2P, 3,3-Diphenylpropylamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
5666-18-2P 14451-09-3P, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
17349-94-9P 19841-73-7P 21745-77-7P, 9H-Xanthene-9-ethanamine
21745-81-3P, 9H-Thioxanthene-9-ethanamine 21745-82-4P 21745-83-5P
21745-85-7P 28075-29-8P 36765-74-9P 48166-95-6P 53179-07-0P
54910-89-3P 57226-64-9P 63940-51-2P 64630-52-0P 90531-05-8P
91472-94-5P 95956-62-0P 98383-47-2P 98383-56-3P 106359-50-6P
109306-10-7P 114754-01-7P 114754-02-8P 114754-03-9P 114754-04-0P
118468-16-9P 144451-90-1P 144451-98-9P 144452-04-0P 144452-11-9P
159149-65-2P 170018-54-9P 170018-55-0P 170018-56-1P 170018-57-2P
170018-63-0P 170018-66-3P 170018-67-4P 170018-68-5P 170018-71-0P
170018-72-1P 170018-73-2P 170018-74-3P 170018-75-4P 170018-76-5P
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170018-82-3P 170018-83-4P 170018-84-5P 170018-85-6P 170018-86-7P

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|---------------------|---------------------|---------------------|---------------------|--------------|
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| 186495-41-0P | 186495-42-1P | 186495-43-2P | 186495-44-3P | 186495-45-4P |
| 186495-46-5P | 186495-47-6P | 186495-48-7P | 186495-49-8P | |
| 186495-50-1P | 186495-51-2P | 186495-52-3P | 186495-53-4P | 186495-54-5P |
| 186495-55-6P | 186495-56-7P | 186495-57-8P | 186495-58-9P | |
| 186495-59-0P | 186495-60-3P | 186495-61-4P | 186495-62-5P | 186495-63-6P |
| 186495-64-7P | 186495-65-8P | 186495-66-9P | 186495-67-0P | 186495-68-1P |
| 186495-69-2P | 186495-70-5P | 186495-71-6P | 186495-72-7P | 186495-73-8P |
| 186495-74-9P | 186495-75-0P | 186495-76-1P | 186495-77-2P | 186495-78-3P |
| 186495-79-4P | 186495-80-7P | 186495-81-8P | 186495-82-9P | 186495-84-1P |
| 186495-86-3P | 186495-87-4P | 186495-88-5P | 186495-89-6P | 186495-90-9P |
| 186495-91-0P | 186495-92-1P | 186495-93-2P | 186495-94-3P | 186495-95-4P |
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| 186496-29-7P | 186496-30-0P | 186496-71-9P | 200420-69-5P | 200427-53-8P |
| 200429-46-5P | 200429-48-7P | 200429-49-8P | 200429-50-1P | 200429-51-2P |
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| 200429-56-7P | 200429-57-8P | 200429-58-9P | 200429-59-0P | 200429-60-3P |
| 200429-61-4P | 200429-62-5P | 200429-63-6P | 200429-64-7P | 200429-65-8P |
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| 200429-71-6P | 200429-72-7P | 200429-73-8P | 200429-74-9P | |
| 200429-75-0P | 200429-79-4P | 200429-80-7P | 200429-86-3P | 200429-87-4P |
| 200430-04-2P | 200430-05-3P | 200430-06-4P | 200430-07-5P | |
| 200430-08-6P | 200430-14-4P | 200430-16-6P | 200430-18-8P | |
| 200430-19-9P | | | | |

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 85-41-6, Phthalimide 103-67-3, N-Methylbenzylamine 135-02-4, o-Anisaldehyde 140-88-5 285-67-6, Cyclopentene oxide 345-70-0, 3,3'-Difluorobenzophenone 351-54-2, 3-Fluoro-p-anisaldehyde 372-20-3, 3-Fluorophenol 452-08-4, 2-Bromo-4-fluoroanisole 456-48-4, 3-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 578-57-4, 2-Bromoanisole 587-04-2, 3-Chlorobenzaldehyde 610-99-1 932-31-0, 2-Methylphenylmagnesium bromide 1073-06-9, 1-Bromo-3-fluorobenzene 1210-35-1, Dibenzosuberone 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one 17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2, (S)-N-Benzyl- α -methylbenzylamine 18707-60-3, Methyl crotonate 20595-30-6, Trans-3-Fluorocinnamic acid 21900-39-0, 5-Fluoro-2-methylbenzoyl chloride 65416-24-2, Benzyl crotonate 77532-79-7, 5-Fluoro-2-methylbenzonitrile 100306-34-1 147624-13-3, 3-Fluoro-2-methylbenzaldehyde 170019-09-7, 3,3-Bis(3-fluorophenyl)propionitrile 186496-59-3, 5-Fluoro-2-methylphenylmagnesium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 455-67-4P 458-45-7P 701-38-2P 5561-92-2P, 1-(2-Methoxyphenyl)-1-propanone 15966-37-7P 21745-42-6P 21745-68-6P 25772-94-5P 38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P 156868-83-6P, 3-(3-Fluorophenyl)-1-propanol 170019-11-1P 170019-14-4P, Ethyl 3,3-bis(3-fluorophenyl)propionate 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P 170019-24-6P 170019-25-7P 186496-34-4P 186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P 186496-40-2P 186496-41-3P 186496-42-4P 186496-44-6P 186496-45-7P 186496-46-8P 186496-48-0P 186496-49-1P 186496-50-4P 186496-51-5P 186496-52-6P 186496-53-7P 186496-57-1P 186496-58-2P 186496-60-6P 200430-09-7P 200430-10-0P 200430-11-1P 200430-12-2P, 3,3'-Difluoro-4-methoxybenzophenone 200430-13-3P 200430-15-5P 200430-17-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

REFERENCE COUNT: 172 THERE ARE 172 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:741905 CAPLUS

DOCUMENT NUMBER: 133:305610

TITLE: Treatment of neurological disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators

INVENTOR(S): O'Neill, Michael John

PATENT ASSIGNEE(S): Eli Lilly and Company Limited, UK

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2000061126 | A2 | 20001019 | WO 2000-GB1284 | 20000406 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: GB 1999-8175 A 19990409

AB The present invention relates to a method of treating a neurol. disorder comprising administering to a patient an effective amount of a nitric oxide synthase inhibitor in combination with an effective amount of an excitatory amino receptor modulator. Combination of 2.5 mg/kg Mk-801, i.p., and 25 mg/kg ARL17477, i.p., had a synergistic degree of neuroprotection (78%) in cerebral ischemia induced in gerbils.

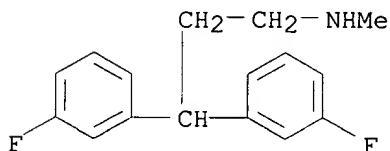
IT 186495-99-8, NPS 1506

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate receptors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AMPA-binding, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate antagonists
(NMDA antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Nervous system
(disease; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Neurotransmitter antagonists
(excitatory amino acid; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Amino acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(excitatory, agonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Brain, disease
(ischemia, focal; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Brain, disease
(ischemia; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kainate-binding, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic, mGluR1, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic, mGluR2, agonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic, mGluR3, agonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabotropic, mGluR5, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Cytoprotective agents
(neuroprotectants; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT 125-71-3, Dextromethorphan 125-73-5 1003-51-6, Ha-966 2942-42-9, 7-Nitroindazole 19982-08-2, Memantine 23210-56-2, Ifenprodil 25371-96-4, 1-(2-Trifluoromethylphenyl)imidazole 74209-34-0, 3-Bromo-7-nitroindazole 77086-22-7, Mk-801 110347-85-8, Cgs 19755 117414-74-1 118876-58-7, Nbqx 119431-25-3, Eliprodil 125546-04-5, Ly233053 137159-92-3, Aptiganel 137160-11-3, Cns1102 143343-70-8,

Ly202157 143692-18-6, Ly300168 151056-97-2, 1701273 153436-38-5, GV
 150526A 153504-81-5, Acea1021 154164-30-4, Ym90k 154652-83-2,
 Ly293558 157971-06-7, GYK 152466 161832-65-1, Ly300164 168895-09-8,
 ARL17477 176199-48-7, Ly 354740 **186495-99-8**, NPS 1506
 191471-52-0, Ly379268 210245-80-0, Ym872 211566-75-5, Ly382884
 222529-89-7, LY 389795 301857-79-4, L-MIN 301857-80-7, Ramacemide
 301857-81-8, LY 377770

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

L5 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:53380 CAPLUS

DOCUMENT NUMBER: 132:93096

TITLE: Preparation of diarylalkylamines and related compounds active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders.

INVENTOR(S): Mueller, Alan; Moe, Scott; Balandrin, Manuel

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2000002551 | A2 | 20000120 | WO 1999-US15857 | 19990712 |
| WO 2000002551 | A3 | 20000921 | | |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2336962 | AA | 20000120 | CA 1999-2336962 | 19990712 |
| AU 9949919 | A1 | 20000201 | AU 1999-49919 | 19990712 |
| AU 771252 | B2 | 20040318 | | |
| EP 1096926 | A2 | 20010509 | EP 1999-933987 | 19990712 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| US 2004039014 | A1 | 20040226 | US 2001-990405 | 20011121 |
| PRIORITY APPLN. INFO.: | | | US 1998-92546P | P 19980713 |
| | | | WO 1999-US15857 | W 19990712 |

OTHER SOURCE(S): MARPAT 132:93096

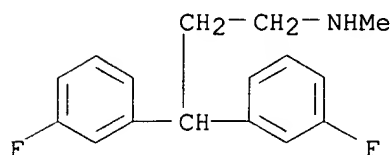
AB A method for treatment of depression comprises administration of a compound having NMDA receptor binding activity of IC50 = 50 nM to 1 µM and serotonin reuptake IC50 ≤100 nM. The compds. include e.g. XmArl(XmArl2)CHCR1R1CR2R2NR3R3 [X = Br, Cl, F, iodo, CF3, alkyl, OH, OCF3, alkoxy, acyloxy; Ar1, Ar2 = Ph, naphthyl, thiofuranyl, tetrahydronaphthyl, furyl, pyridyl, etc.; R1 = H, alkyl, hydroxyalkyl, OH, alkoxy, acyloxy; R2 = H, alkyl, hydroxyalkyl; (R2)2 = imino; R3 = H, alkyl, HOCH2CH2, alkylphenyl; m = 0-5]. Thus, N-methyl-bis-[3-(3-fluorophenyl)]propylamine (preparation given) at 5 mg/kg orally in mice produced a time-dependent reduction in the duration of immobility in the forced swimming test.

IT **186495-99-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

RN 186495-99-8 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists
(NMDA antagonists; preparation of diarylalkylamines and related compds.
active at both the serotonin reuptake site and the N-methyl-D-aspartate
receptor for treatment depression and other disorders)

IT Antidepressants
(preparation of diarylalkylamines and related compds. active at both the
serotonin reuptake site and the N-methyl-D-aspartate receptor for
treatment depression and other disorders)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
(Miscellaneous); BIOL (Biological study); PROC (Process)
(reuptake inhibitors; preparation of diarylalkylamines and related compds.
active at both the serotonin reuptake site and the N-methyl-D-aspartate
receptor for treatment depression and other disorders)

IT 21745-82-4P 21745-83-5P 50366-32-0P 186495-87-4P
186495-99-8P 186496-01-5P 200429-75-0P 200430-07-5P
255039-63-5P 255039-64-6P 255039-65-7P 255039-66-8P 255039-67-9P
255039-68-0P 255039-69-1P 255039-70-4P 255039-71-5P 255039-72-6P
255039-73-7P 255039-74-8P 255039-75-9P 255039-76-0P 255039-77-1P
255039-78-2P 255039-79-3P 255039-80-6P 255039-81-7P 255039-82-8P
255040-00-7P 255040-01-8P 255040-02-9P 255040-03-0P 255040-04-1P
255040-05-2P 255040-07-4P 255040-08-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diarylalkylamines and related compds. active at both the
serotonin reuptake site and the N-methyl-D-aspartate receptor for
treatment depression and other disorders)

IT 74-89-5, Methylamine, reactions 95-48-7, reactions 103-67-3,
N-Benzylmethylamine 140-88-5 345-69-7, 3-Fluorobenzophenone
345-70-0, 3,3'-Difluorobenzophenone 372-20-3, 3-Fluorophenol 395-23-3,
4-Trifluoromethylbenzhydrol 402-45-9, p-Trifluoromethylphenol
457-68-1, 4,4'-Difluorodiphenylmethane 529-20-4, o-Tolualdehyde
540-51-2, 2-Bromoethanol 590-17-0, Bromoacetonitrile 625-36-5,
3-Chloropropionyl chloride 932-31-0, o-Tolylmagnesium bromide
933-88-0, o-Toluoyl chloride 1073-06-9, 3-Bromofluorobenzene
1210-35-1, Dibenzosuberone 2537-48-6, Diethyl cyanomethylphosphonate
20595-30-6, trans-3-Fluorocinnamic acid 72551-53-2 100306-33-0
100306-34-1 186496-23-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diarylalkylamines and related compds. active at both the
serotonin reuptake site and the N-methyl-D-aspartate receptor for
treatment depression and other disorders)

IT 365-17-3P 458-45-7P 1018-97-9P 15966-37-7P 25772-94-5P
38158-75-7P 50499-52-0P 53915-75-6P 69096-48-6P 83406-26-2P
84648-43-1P 98586-21-1P 156868-83-6P 186496-49-1P 186496-50-4P
186496-57-1P 186496-58-2P 186496-60-6P 200430-09-7P 200430-10-0P
200430-17-7P 255039-83-9P 255039-84-0P 255039-85-1P 255039-86-2P
255039-87-3P 255039-88-4P 255039-89-5P 255039-90-8P 255039-91-9P
255039-92-0P 255039-93-1P 255039-94-2P 255039-95-3P 255039-96-4P
255039-97-5P 255039-98-6P 255039-99-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of diarylalkylamines and related compds. active at both the serotonin reuptake site and the N-methyl-D-aspartate receptor for treatment depression and other disorders)

L5 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:814825 CAPLUS

DOCUMENT NUMBER: 135:55870

TITLE: NPS 1506 Attenuates Cognitive Dysfunction and Hippocampal Neuron Death Following Brain Trauma in the Rat

AUTHOR(S): Leoni, Matthew J.; Chen, Xiao-Han; Mueller, Alan L.; Cheney, Jessica; McIntosh, Tracy K.; Smith, Douglas H.

CORPORATE SOURCE: Department of Neurosurgery, University of Pennsylvania, Philadelphia, PA, 19104, USA

SOURCE: Experimental Neurology (2000), 166(2), 442-449
CODEN: EXNEAC; ISSN: 0014-4886

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although several noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonists have been shown to be substantially efficacious in exptl. models of brain trauma, side effects associated with this class of compds. have impeded clin. application. Therefore, new noncompetitive NMDA receptor antagonists have been developed, including NPS 1506, that appear to be nontoxic but retain efficacy. In the present study, we evaluated the efficacy of NPS 1506 in a model of parasagittal fluid percussion brain trauma in the anesthetized rat. Administration of 1 mg/kg NPS 1506 at both 10 min and 4 h posttrauma induced no changes in brain temperature, mean arterial pressure, pulse, or arterial blood gasses. At 1 wk postinjury, animals treated with the same dosing regimen of NPS 1506 demonstrated a dramatic attenuation of memory dysfunction evaluated by a water maze task and had greatly reduced neuron death in the CA3 subfield of the hippocampus. However, NPS 1506 treatment did not significantly affect the extent of cortical tissue loss following injury. Since memory dysfunction and hippocampal damage are common and potentially related consequences of brain trauma in humans, our results suggest that NPS 1506 treatment may have clin. utility. (c) 2000 Academic Press.

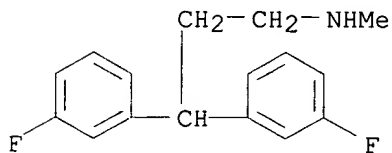
IT 186495-99-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Cognition enhancers

(NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

IT Memory, biological

(disorder; NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

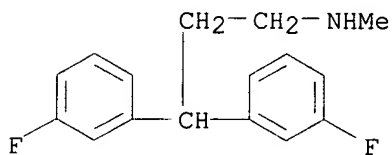
IT Brain, disease

(hippocampus, injury; NPS 1506 attenuates cognitive dysfunction and

hippocampal neuron death following brain trauma in rats)
 IT Cytoprotective agents
 (neuroprotectants; NPS 1506 attenuates cognitive dysfunction and
 hippocampal neuron death following brain trauma in rats)
 IT Brain, disease
 (trauma; NPS 1506 attenuates cognitive dysfunction and hippocampal
 neuron death following brain trauma in rats)
 IT **186495-99-8**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death
 following brain trauma in rats)
 REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2000:740404 CAPLUS
 DOCUMENT NUMBER: 134:95398
 TITLE: NPS 1506, a moderate affinity uncompetitive NMDA
 receptor antagonist: preclinical summary and clinical
 experience
 AUTHOR(S): Mueller, A. L.; Artman, L. D.; Balandrin, M. F.;
 Brady, E.; Chien, Y.; DelMar, E. G.; Kierstead, A.;
 Marriott, T. B.; Moe, S. T.; Raszkiewicz, J. L.; Van
 Wagenen, B.; Wells, D.
 CORPORATE SOURCE: NPS Pharmaceuticals, Inc., Salt Lake City, UT, USA
 SOURCE: Amino Acids (2000), 19(1), 177-179
 CODEN: AACIE6; ISSN: 0939-4451
 PUBLISHER: Springer-Verlag Wien
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB NPS Pharmaceuticals, Inc. (NPS) has synthesized a series of open-channel
 blockers with varying potencies at the NMDA receptor. NPS 1506 is a
 moderate affinity antagonist that inhibits NMDA/glycine-induced increases
 in cytosolic calcium in cultured rat cerebellar granule cells (IC50 =
 476nM) and displaces the binding of [3H]MK-801 to rat cortical membranes
 (IC50 = 664nM).
 IT **186495-99-8**, NPS 1506
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
 BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); PROC (Process); USES (Uses)
 (NPS 1506, a NMDA receptor antagonist, preclin. summary and clin.
 experience)
 RN 186495-99-8 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
 hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists
 (NMDA antagonists; NPS 1506 a NMDA receptor antagonist, preclin.
 summary and clin. experience)
 IT Cytoprotective agents
 (neuroprotectants; NPS 1506 a NMDA receptor antagonist, preclin.
 summary and clin. experience)
 IT **186495-99-8**, NPS 1506
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process);

BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); PROC (Process); USES (Uses)
(NPS 1506, a NMDA receptor antagonist, preclin. summary and clin.
experience)

L5 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:388157 CAPLUS

DOCUMENT NUMBER: 131:44658

TITLE: Preparation of bis(fluorophenyl)alkylamides as
anticonvulsants and central nervous system agents.

INVENTOR(S): Balandrin, Manuel F.; Vanwagenen, Bradford C.; Artman,
Linda D.; Mueller, Alan L.; Smith, Daryl

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

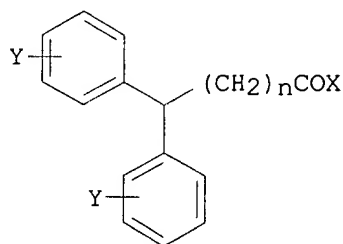
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9929657 | A1 | 19990617 | WO 1998-US26315 | 19981209 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2313236 | AA | 19990617 | CA 1998-2313236 | 19981209 |
| AU 9918170 | A1 | 19990628 | AU 1999-18170 | 19981209 |
| AU 763245 | B2 | 20030717 | | |
| EP 1042275 | A1 | 20001011 | EP 1998-963065 | 19981209 |
| EP 1042275 | B1 | 20051109 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001525390 | T2 | 20011211 | JP 2000-524254 | 19981209 |
| NZ 524395 | A | 20041029 | NZ 1998-524395 | 19981209 |
| IL 136306 | A1 | 20050925 | IL 1998-136306 | 19981209 |
| AT 309200 | E | 20051115 | AT 1998-963065 | 19981209 |
| US 6617358 | B1 | 20030909 | US 2000-587179 | 20000602 |
| US 2003199589 | A1 | 20031023 | US 2003-429060 | 20030502 |
| PRIORITY APPLN. INFO.: | | | US 1997-69005P | P 19971210 |
| | | | WO 1998-US26315 | W 19981209 |
| | | | US 2000-587179 | A1 20000602 |

OTHER SOURCE(S): MARPAT 131:44658
GI



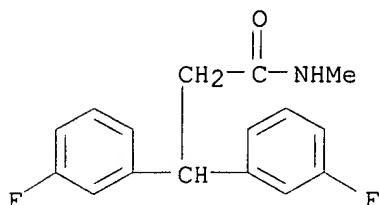
AB Title compds. (I; Y = H, F, Cl; X = NR₁R₂, OR₁; R₁ = H, alkyl, hydroxyalkyl; R₂ = H, Me, Et; n = 0-4; with specific exceptions), were prepared for treatment of seizure disorder, neurodegenerative disease, anxiety, stress, multiple sclerosis, Parkinson's disease, migraine, etc. (no data). Thus, 4,4-bis(4-fluorophenyl)butyl chloride was treated successively with KOAc in DMF, NaOH in EtOH/H₂O, CrO₃/H₂SO₄ in

H2O/acetone, SOCl2, and NH3 in H2O/EtOAc to give 4,4-bis(4-fluorophenyl)butanamide.

IT **200429-55-6P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

RN 200429-55-6 CAPLUS

CN Benzenepropanamide, 3-fluoro-β-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



IT Nervous system
 (Huntington's chorea, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Nervous system
 (amyotrophic lateral sclerosis, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Spinal cord
 (injury, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (manic bipolar disorder, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Mental disorder
 (mood-affecting, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Anti-Alzheimer's agents
 Anticonvulsants
 Antimigraine agents
 Antiparkinsonian agents
 Anxiolytics
 Nervous system agents
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Brain, disease
 (stroke, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Head
 (trauma, treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT Multiple sclerosis
 (treatment; preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 51787-97-4P 170019-23-5P 200429-51-2P 200429-52-3P 200429-53-4P
 200429-54-5P **200429-55-6P** 227289-95-4P 227290-02-0P
 227290-09-7P 227290-12-2P 227290-22-4P 227290-28-0P 227290-37-1P
 227290-41-7P 227290-47-3P 227290-50-8P 227290-56-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central nervous system agents)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions
 124-68-5 345-70-0, 3,3'-Difluorobenzophenone 345-92-6,
 4,4'-Difluorobenzophenone 365-24-2, 4,4'-Difluorobenzhydrol 623-71-2,

Ethyl 3-chloropropionate 625-98-9, 3-Fluorochlorobenzene 867-13-0,
Triethyl phosphonoacetate 2537-48-6, Diethyl cyanomethylphosphonate
3312-04-7, 4,4-Bis(4-fluorophenyl)butyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central
nervous system agents)

IT 361-63-7P 20662-52-6P 50337-85-4P 50481-36-2P 50775-35-4P
50775-37-6P, 3,3-Bis(4-fluorophenyl)propionitrile 54167-10-1P
170019-14-4P 170019-22-4P 227290-57-5P, 1-Acetoxy-4,4-bis(3-
fluorophenyl)butane 227290-60-0P 227290-62-2P 227290-63-3P
227290-64-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of bis(fluorophenyl)alkylamides as anticonvulsants and central
nervous system agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:74531 CAPLUS

DOCUMENT NUMBER: 132:342594

TITLE: NPS 1506, a novel NMDA receptor antagonist and
neuroprotectant: Review of preclinical and clinical
studies

AUTHOR(S): Mueller, Alan L.; Artman, Linda D.; Balandrin, Manuel
F.; Brady, Ellen; Chien, Yongwei; Delmar, Eric G.;
George, Karen; Kierstead, Allison; Marriott, Thomas
B.; Moe, Scott T.; Newman, Michael K.; Raszkiewicz,
Joanna L.; Sanguinetti, Elizabeth L.; Van Wagenen,
Bradford C.; Wells, David

CORPORATE SOURCE: NPS Pharmaceuticals, Inc., Salt Lake City, UT, 84108,
USA

SOURCE: Annals of the New York Academy of Sciences (1999),
890(Neuroprotective Agents), 450-457
CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 10 refs. NPS 1506 is a moderate-affinity, uncompetitive
N-methyl-D-aspartate (NMDA) receptor antagonist. NPS 1506 is
neuroprotective in rodent models of ischemic stroke, hemorrhagic stroke,
and head trauma, with a 2-h window of opportunity. Neuroprotectant doses
of NPS 1506 ranged approx. 0.1-1.0 mg/kg, with peak plasma concns. of 8-80
ng/mL. Even at doses producing behavioral toxicity, NPS 1506 did not
elicit MK-801-like behaviors, did not generalize to phencyclidine (PCP),
and did not elicit neuronal vacuolization. In a Phase I study, i.v. doses
of NPS 1506 of 5-100 mg were well tolerated and provided plasma concns. in
excess of those required for neuroprotection in rodents. Adverse events
at the 100-mg dose included mild dizziness and lightheadedness, and mild
to moderate ataxia. Neither PCP-like psychotomimetic effects nor
cardiovascular effects were noted. The long plasma half-life of NPS 1506
(.apprx.60 h) suggests that a single i.v. dose will provide prolonged
neuroprotection in humans.

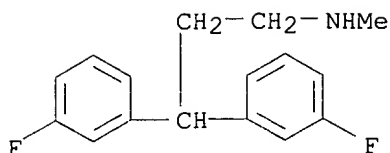
IT 186495-99-8, NPS 1506

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
effector, except adverse); BPR (Biological process); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC
(Process); USES (Uses)

(NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists
(NMDA antagonists; NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

IT Cytoprotective agents
(neuroprotectants; NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

IT **186495-99-8**, NPS 1506
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (NPS 1506, a novel NMDA receptor antagonist and neuroprotectant)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:7958 CAPLUS

DOCUMENT NUMBER: 130:66268

TITLE: Compounds active at a novel site on receptor-operated calcium channels useful for treatment of neurological disorders and diseases

INVENTOR(S): Mueller, Alan L.; Moe, Scott T.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 252 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| WO 9856752 | A1 | 19981217 | WO 1998-US11608 | 19980611 |
| W: JP | | | | |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| PRIORITY APPLN. INFO.: | | | US 1997-873011 | A 19970611 |
| | | | AU 1997-13525 | A3 19961211 |

OTHER SOURCE(S): MARPAT 130:66268

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The compds. [I, II, III; R1 and R3 are independently selected from (un)substituted Ph, benzyl, phenoxy, H, alkyl, OH, etc.; R2 and R5 are independently selected from H, alkyl, hydroxyalkyl; R2-R5 together are imino; R1-R2 together are (CH2)n, (CH2)n-N(R6)-(CH2)n; n = 0-6, at least one n greater than 0; R6 is H, alkyl, 2-hydroxyethyl, and alkylphenyl; R4 is selected from (un)substituted thiofuryl, pyridyl, Ph, benzyl, phenoxy, phenylthio, H, alkyl, chcloalkyl; X, X1 is independently selected from (un)substituted Ph, benzyl, phenoxy, F, Cl, Br, Oh, etc.; m = 0-5; Y is N(R6)2, H when R1-R2 together are (CH2)n-N(R6)-(CH2)n], pharmaceutical compns., and pharmaceutical acceptable salts, complexes, and carriers are prepared as antagonists of NMDA receptor-mediated responses for treating a neurol. disease or disorder such as stroke, head trauma, spinal cord

injury, spinal cord ischemia, ischemia- or hypoxia-induced nerve cell damage, epilepsy, anxiety, neuropsychiatric or cognitive deficits due to ischemia or hypoxia such as those that frequently occur as a consequence of cardiac surgery under cardiopulmonary bypass, or neurodegenerative diseases such as Alzheimer's Disease, Huntington's Disease, Parkinson's Disease, or amyotrophic lateral sclerosis (ALS).

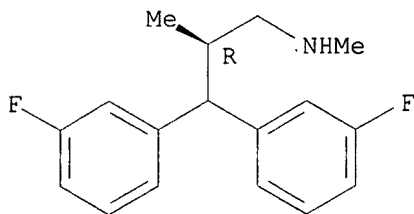
IT 186495-55-6P 186495-56-7P 186495-99-8P
200429-55-6P 200430-06-4P 200430-16-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

RN 186495-55-6 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-, (β R)- (9CI) (CA INDEX NAME)

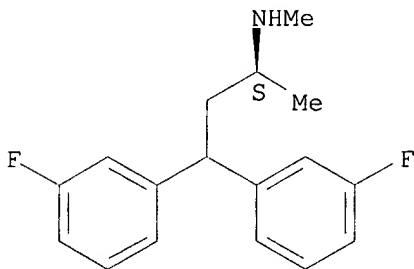
Absolute stereochemistry.



RN 186495-56-7 CAPLUS

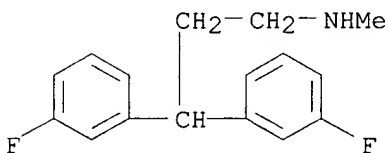
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186495-99-8 CAPLUS

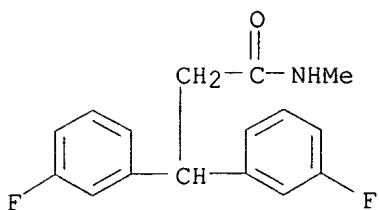
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)



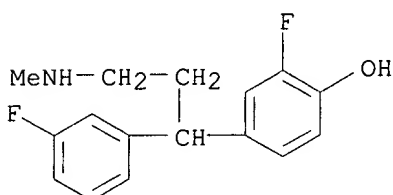
● HCl

RN 200429-55-6 CAPLUS

CN Benzenepropanamide, 3-fluoro- β -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 200430-06-4 CAPLUS
 CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]-, hydrochloride (9CI) (CA INDEX NAME)

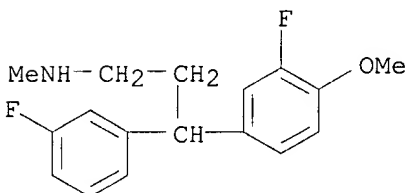


● HCl

RN 200430-16-6 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

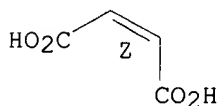
CRN 200429-70-5
 CMF C17 H19 F2 N O



CM 2

CRN 110-16-7
 CMF C4 H4 O4

Double bond geometry as shown.



IT Glutamate receptors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (NMDA-binding; compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT Amines, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(aralkyl; compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT Asymmetric synthesis and induction
Drug delivery systems
(compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT Nervous system
(disease; compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 5586-73-2P 170018-57-2P 186495-38-5P 200430-19-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
5666-18-2P 14451-09-3P, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
17349-94-9P 19841-73-7P 21745-77-7P, 9H-Xanthene-9-ethanamine
21745-81-3P, 9H-Thioxanthene-9-ethanamine 21745-82-4P 28075-29-8P
36765-74-9P 48166-95-6P 53179-07-0P 54910-89-3P 57226-64-9P
63940-51-2P 64630-52-0P 90531-05-8P 91472-94-5P 95956-62-0P
98383-47-2P 98383-56-3P 106359-50-6P 109306-10-7P 114754-01-7P
114754-02-8P 114754-03-9P 114754-04-0P 116541-62-9P 118468-16-9P
144451-90-1P 144452-11-9P 159149-65-2P 170018-39-0P 170018-44-7P
170018-46-9P 170018-47-0P 170018-48-1P 170018-49-2P 170018-50-5P
170018-51-6P 170018-52-7P 170018-55-0P 170018-56-1P 170018-63-0P
170018-68-5P 170018-71-0P 170018-72-1P 170018-73-2P 170018-74-3P
170018-75-4P 170018-76-5P 170018-77-6P 170018-78-7P 170018-79-8P
170018-80-1P 170018-81-2P 170018-82-3P 170018-84-5P 170018-85-6P
170018-86-7P 186495-39-6P 186495-40-9P 186495-41-0P 186495-42-1P
186495-44-3P 186495-48-7P 186495-50-1P 186495-51-2P 186495-53-4P
186495-55-6P 186495-56-7P 186495-57-8P 186495-58-9P
186495-59-0P 186495-60-3P 186495-61-4P 186495-62-5P 186495-65-8P
186495-66-9P 186495-67-0P 186495-68-1P 186495-69-2P 186495-70-5P
186495-71-6P 186495-72-7P 186495-73-8P 186495-74-9P 186495-75-0P
186495-76-1P 186495-77-2P 186495-78-3P 186495-79-4P 186495-80-7P
186495-81-8P 186495-82-9P 186495-84-1P 186495-86-3P 186495-88-5P
186495-89-6P 186495-90-9P 186495-91-0P 186495-93-2P 186495-94-3P
186495-95-4P 186495-97-6P **186495-99-8P** 186496-00-4P
186496-01-5P 186496-02-6P 186496-04-8P 186496-05-9P 186496-06-0P
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186496-13-9P 186496-14-0P 186496-15-1P 186496-16-2P 186496-17-3P
186496-21-9P 186496-22-0P 186496-23-1P 186496-24-2P 186496-25-3P
186496-26-4P 186496-27-5P 186496-29-7P 186496-30-0P 186496-71-9P
200420-69-5P 200427-53-8P 200429-49-8P 200429-50-1P 200429-51-2P
200429-52-3P 200429-53-4P 200429-54-5P **200429-55-6P**
200429-56-7P 200429-57-8P 200429-58-9P 200429-59-0P 200429-60-3P
200429-61-4P 200429-62-5P 200429-63-6P 200429-64-7P 200429-65-8P
200429-67-0P 200429-69-2P 200429-73-8P 200429-74-9P 200429-75-0P
200429-76-1P 200429-77-2P 200429-81-8P 200429-82-9P 200429-84-1P
200430-05-3P **200430-06-4P** 200430-08-6P **200430-16-6P**
200430-18-8P 217658-85-0P 217658-89-4P 217658-94-1P 217658-96-3P
217659-01-3P 217659-23-9P 217659-76-2P 217660-61-2P 217660-91-8P
217660-94-1P 217661-05-7P 217661-16-0P 217661-17-1P 217661-22-8P
217661-23-9P 217661-24-0P 217661-26-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compds. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 50-47-5, Desipramine 50-48-6 50-49-7, Imipramine 50-53-3,
Chlorpromazine, biological studies 58-73-1 59-32-5, Chloropyramine
72-69-5, Nortriptyline 82-92-8, Cyclizine 82-93-9, Chlorcyclizine

86-21-5 86-22-6 113-92-8 144-11-6, Trihexyphenidyl 303-49-1,
Clomipramine 303-53-7, Cyclobenzaprine 390-64-7, Prenylamine
438-60-8, Protriptyline 511-45-5, Pridinol 562-10-7 841-77-0,
Nor-cyclizine 1668-19-5, Doxepin 2062-78-4, Pimozide 2095-87-6
3416-26-0, Lidoflazine 3737-09-5, Disopyramide 3963-62-0 7492-32-2,
Isopropamide 10262-69-8, Maprotiline 56775-88-3, Zimeldine
108393-62-0 108448-58-4 133805-32-0 142275-74-9 144576-90-9
148920-48-3 217661-25-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 170018-54-9P 170019-10-0P

RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 95-46-5, 2-Bromotoluene 100-39-0 103-67-3 105-34-0 135-02-4
140-88-5 285-67-6, Cyclopentene oxide 345-70-0 351-54-2 456-48-4
529-20-4 587-04-2 610-99-1 925-90-6, Ethyl magnesium bromide
1073-06-9 1210-35-1 2537-48-6, Diethyl cyanomethylphosphonate
2627-86-3 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one 17318-03-5,
3-Fluorophenyl magnesium bromide 20595-30-6 21900-39-0 22115-41-9
65416-24-2 77532-79-7 100306-33-0 147624-13-3 170019-09-7
186496-59-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

IT 458-45-7P 1018-97-9P 1799-19-5P 1799-29-7P 2845-91-2P 5561-92-2P
15966-37-7P 17480-69-2P 21745-42-6P 21745-68-6P 25772-94-5P
32019-30-0P 34841-35-5P 38158-77-9P 75762-57-1P 84648-43-1P
93559-81-0P 98586-06-2P 98586-21-1P 125025-34-5P 156868-83-6P
170019-11-1P 170019-12-2P 170019-13-3P 170019-14-4P 170019-15-5P
170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P 170019-21-3P
170019-22-4P, Ethyl 3,3-bis(3-fluorophenyl)acrylate 170019-23-5P,
3,3-Bis(3-fluorophenyl)propionic acid 170019-24-6P, 4,4-Bis(3-
fluorophenyl)-2-butanone 170019-25-7P 186496-31-1P 186496-32-2P
186496-33-3P 186496-34-4P 186496-35-5P 186496-36-6P 186496-37-7P
186496-38-8P 186496-39-9P 186496-40-2P 186496-41-3P 186496-42-4P
186496-43-5P 186496-44-6P 186496-45-7P 186496-46-8P 186496-47-9P
186496-48-0P 186496-49-1P 186496-50-4P 186496-54-8P 186496-55-9P
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217661-28-4P 217661-29-5P 217661-30-8P 217661-31-9P 217661-32-0P
217661-33-1P 217661-34-2P 217661-35-3P 217661-40-0P 217661-42-2P
217661-44-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(comps. active at novel site on receptor-operated calcium channels useful for treatment of neurol. disorders and diseases)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:1444 CAPLUS

DOCUMENT NUMBER: 128:61341

TITLE: Preparation of aralkylamines as NMDA
receptor-ionophore complex antagonists

INVENTOR(S): Mueller, Alan L.; Moe, Scott T.; Balandrin, Manuel F.;
Vanwagenen, Bradford C.; Delmar, Eric G.; Artman,
Linda D.; Barmore, Robert M.; Smith, Daryl L.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 298 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9746511 | A1 | 19971211 | WO 1996-US20697 | 19961211 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2257234 | AA | 19971211 | CA 1996-2257234 | 19961211 |
| AU 9713525 | A1 | 19980105 | AU 1997-13525 | 19961211 |
| AU 723349 | B2 | 20000824 | | |
| EP 912494 | A1 | 19990506 | EP 1996-945069 | 19961211 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002511835 | T2 | 20020416 | JP 1998-500538 | 19961211 |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1996-663013 | A 19960607 |
| | | | WO 1996-US19525 | A 19961206 |
| | | | AU 1997-13525 | A3 19961211 |
| | | | WO 1996-US20697 | W 19961211 |

OTHER SOURCE(S): MARPAT 128:61341

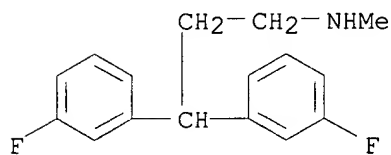
AB R7CHR4CR1R5CRR2R6 [I; R = H or N(R3)2; R1,R5 = (un)substituted Ph, -CH2Ph, -OPh; R2,R6 = H or (hydroxy)alkyl; R1R2 = (CH2)n or (CH2)nNR3(CH2)n; R2R6 = NH; R3 = H, alkyl, CH2CH2OH, alkylphenyl; R4 = (un)substituted Ph, -pyridyl, -thienyl, etc.; R7 = (un)substituted Ph; n = 0-6] were prepared. Thus, (3-FC6H4)2CO was condensed with (EtO)2P(O)CH2CO2Et and the product converted in 6 steps to (3-FC6H4)2CHCH2CHMeNH2. Data for biol. activity of I were given.

IT **186495-49-8P 186495-55-6P 186495-56-7P****186495-99-8P 200429-55-6P 200429-70-5P****200429-72-7P 200430-06-4P 200430-16-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

RN 186495-49-8 CAPLUS

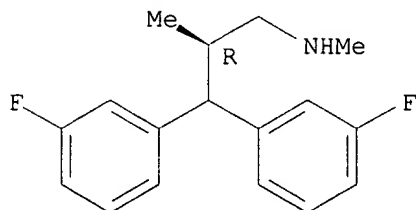
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 186495-55-6 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-, (β R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

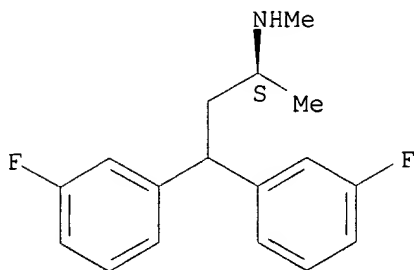


RN 186495-56-7 CAPLUS

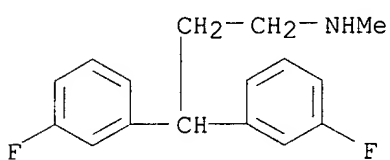
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-,

(α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

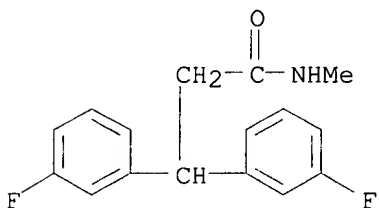


RN 186495-99-8 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)

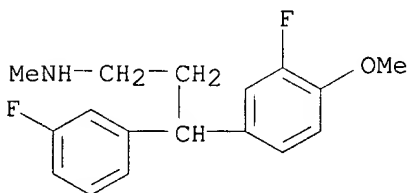


● HCl

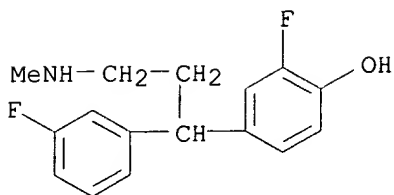
RN 200429-55-6 CAPLUS
CN Benzenepropanamide, 3-fluoro- β -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



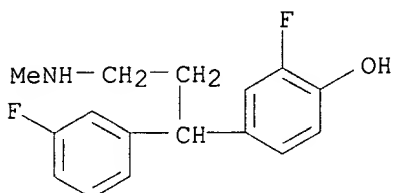
RN 200429-70-5 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-4-methoxy-N-methyl- (9CI) (CA INDEX NAME)



RN 200429-72-7 CAPLUS
CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylamino)propyl]- (9CI) (CA INDEX NAME)



RN 200430-06-4 CAPLUS
 CN Phenol, 2-fluoro-4-[1-(3-fluorophenyl)-3-(methylanino)propyl]-,
 hydrochloride (9CI) (CA INDEX NAME)

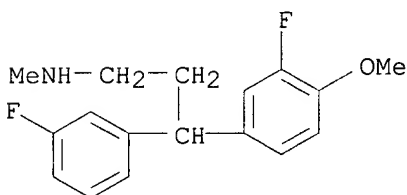


● HCl

RN 200430-16-6 CAPLUS
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-4-methoxy-N-methyl-,
 (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

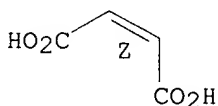
CRN 200429-70-5
 CMF C17 H19 F2 N O



CM 2

CRN 110-16-7
 CMF C4 H4 O4

Double bond geometry as shown.



IT Calcium channel
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (NMDA-binding glutamate receptor complex, antagonists; preparation of
 aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(NMDA-binding, calcium channel complexes, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Glutamate receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(methyl-D-aspartate-binding, calcium channel complexes, antagonists; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Cytoprotective agents

(neuroprotectants; preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT Analgesics

Anticonvulsants

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

IT 5586-73-2P, 3,3-Diphenylpropylamine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex antagonists)

| | | | | | |
|----|---------------------|------------------------------|--|--------------------------|--------------|
| IT | 1140-29-0P | 4361-43-7P | 4646-55-3P | 5341-16-2P | 5415-80-5P |
| | 5666-18-2P | 14451-09-3P | 5H-Dibenzo[a,d]cycloheptene-5-ethanamine | | |
| | 17349-94-9P | 19841-73-7P | 21745-77-7P | 9H-Xanthene-9-ethanamine | |
| | 21745-81-3P | 9H-Thioxanthene-9-ethanamine | 21745-82-4P | 21745-83-5P | |
| | 21745-85-7P | 28075-29-8P | 36765-74-9P | 48166-95-6P | 53179-07-0P |
| | 54910-89-3P | 57226-64-9P | 63940-51-2P | 64630-52-0P | 90531-05-8P |
| | 91472-94-5P | 95956-62-0P | 98383-47-2P | 98383-56-3P | 106359-50-6P |
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| | 118468-16-9P | 144451-90-1P | 144451-98-9P | 144452-04-0P | 144452-11-9P |
| | 159149-65-2P | 170018-54-9P | 170018-55-0P | 170018-56-1P | 170018-57-2P |
| | 170018-63-0P | 170018-66-3P | 170018-67-4P | 170018-68-5P | 170018-71-0P |
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| | 200429-56-7P | 200429-57-8P | 200429-58-9P | 200429-59-0P | 200429-60-3P |
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| | 200430-14-4P | 200430-16-6P | 200430-18-8P | 200430-19-9P | |

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

IT 85-41-6, Phthalimide 103-67-3, N-Methylbenzylamine 135-02-4,
o-Anisaldehyde 140-88-5 285-67-6, Cyclopentene oxide 345-70-0,
3,3'-Difluorobenzophenone 351-54-2, 3-Fluoro-p-anisaldehyde 372-20-3,
3-Fluorophenol 452-08-4, 2-Bromo-4-fluoroanisole 456-48-4,
3-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 578-57-4,
2-Bromoanisole 587-04-2, 3-Chlorobenzaldehyde 610-99-1 932-31-0,
2-Methylphenylmagnesium bromide 1073-06-9, 1-Bromo-3-fluorobenzene
1210-35-1, Dibenzosuberone 4504-87-4, Dibenz[b,e]oxepin-11(6H)-one
17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2,
(S)-N-Benzyl- α -methylbenzylamine 18707-60-3, Methyl crotonate
20595-30-6, trans-3-Fluorocinnamic acid 21900-39-0, 5-Fluoro-2-
methylbenzoyl chloride 65416-24-2, Benzyl crotonate 77532-79-7,
5-Fluoro-2-methylbenzonitrile 100306-34-1 147624-13-3,
3-Fluoro-2-methylbenzaldehyde 170019-09-7, 3,3-Bis(3-
fluorophenyl)propionitrile 186496-59-3, 5-Fluoro-2-methylphenylmagnesium
bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

IT 455-67-4P 458-45-7P 701-38-2P 5561-92-2P, 1-(2-Methoxyphenyl)-1-
propanone 15966-37-7P 21745-42-6P 21745-68-6P 25772-94-5P
38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P
156868-83-6P, 3-(3-Fluorophenyl)-1-propanol 170019-11-1P 170019-14-4P,
Ethyl 3,3-bis(3-fluorophenyl)propionate 170019-15-5P 170019-16-6P
170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P 170019-21-3P
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200430-09-7P 200430-10-0P 200430-11-1P 200430-12-2P,
3,3'-Difluoro-4-methoxybenzophenone 200430-13-3P 200430-15-5P
200430-17-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of aralkylamines as NMDA receptor-ionophore complex
antagonists)

L5 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:132773 CAPLUS

DOCUMENT NUMBER: 126:143970

TITLE: Preparation of 1-amino-3,3-diphenylpropanes and
related compounds as noncompetitive antagonists of
glutamate receptor operated calcium channels in the
central nervous system.

INVENTOR(S): Mueller, Alan L.; Moe, Scott T.; Balandrin, Manuel F.;
Delmar, Eric G.; Vanwagenen, Bradford C.; Artman,
Linda D.; Barmore, Robert M.; Smith, Daryl L.

PATENT ASSIGNEE(S): Nps Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 313 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

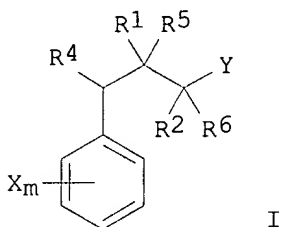
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9640097 | A1 | 19961219 | WO 1996-US10201 | 19960607 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 6071970 | A | 20000606 | US 1995-485038 | 19950607 |

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|---|----|----------|----------------|----------|
| AU 9661125 | A1 | 19961230 | AU 1996-61125 | 19960607 |
| AU 716122 | B2 | 20000217 | | |
| EP 831799 | A1 | 19980401 | EP 1996-918477 | 19960607 |
| EP 831799 | B1 | 20030502 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 11506469 | T2 | 19990608 | JP 1996-502238 | 19960607 |
| BR 9609019 | A | 19990706 | BR 1996-9019 | 19960607 |
| NZ 310344 | A | 20010330 | NZ 1996-310344 | 19960607 |
| AT 238782 | E | 20030515 | AT 1996-918477 | 19960607 |
| PL 185492 | B1 | 20030530 | PL 1996-323871 | 19960607 |
| RU 2246300 | C2 | 20050220 | RU 1998-100454 | 19960607 |
| HK 1008980 | A1 | 20031107 | HK 1998-109748 | 19980806 |
| AU 770292 | B2 | 20040219 | AU 2000-71810 | 20001124 |

PRIORITY APPLN. INFO.:

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|-----------------|----|----------|
| US 1995-485038 | A | 19950607 |
| US 1993-14813 | B2 | 19930208 |
| US 1994-194210 | B2 | 19940208 |
| US 1994-288668 | B2 | 19940809 |
| WO 1994-US12293 | A2 | 19941026 |
| WO 1996-US10201 | W | 19960607 |
| AU 1997-13525 | A3 | 19961211 |

OTHER SOURCE(S): MARPAT 126:143970
GI



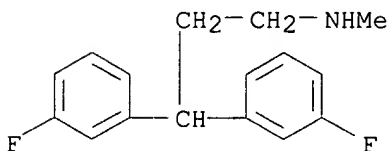
AB Title compds. [I; R1, R5 = H, OH, alkyl, hydroxyalkyl, alkoxy, acyloxy, (substituted) Ph, PhCH2, PhO; R2, R6 = H, alkyl, hydroxyalkyl; R2R4 = imino, (CH2)n, (CH2)nNR3(CH2)n; R3 = H, alkyl, HOCH2CH2, alkylphenyl; n = 0-6, only 1 n can = 0; R4 = (substituted) thiofuryl, pyridyl, Ph, PhCH2, PhO, PhS; X = (substituted) Ph, PhCH2, PhO; m = 0-5; Y = N(R3)2; when R1R2 = (CH2)nNR3(CH2)n, then Y = H], were prepared Thus, di-Et cyanomethylphosphonate was stirred 4 h with NaH in dimethoxyethane; 3,3'-difluorobenzophenone in dimethoxyethane was added and the mixture was stirred 24 h at room temperature to give the cyanomethyl carbinol, which was hydrogenated to give an aminopropanol which was dehydrated and hydrogenated to give 3,3-bis(3-fluorophenyl)propylamine hydrochloride. The latter showed anticonvulsant activity against electroshock-induced seizures in mice with ED50 = 20.1 mg/kg i.p.

IT **186495-49-8P 186495-55-6P 186495-56-7P 186495-99-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

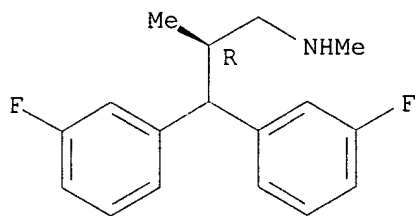
RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



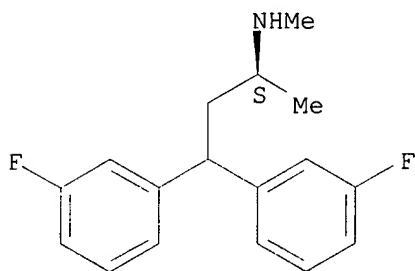
RN 186495-55-6 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-,
(β R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

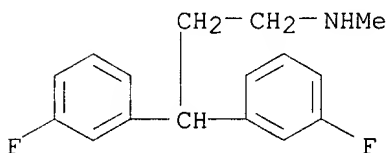


RN 186495-56-7 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-,
(α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186495-99-8 CAPLUS
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT Glutamate antagonists
(NMDA antagonists; preparation of 1-amino-3,3-diphenylpropanes and related
compds. as noncompetitive antagonists of glutamate receptor operated
calcium channels in the central nervous system)

IT Calcium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of 1-amino-3,3-diphenylpropanes and related compds.
as noncompetitive antagonists of glutamate receptor operated calcium
channels in the central nervous system)

IT Cytoprotective agents
(neuroprotectants; preparation of 1-amino-3,3-diphenylpropanes and related
compds. as noncompetitive antagonists of glutamate receptor operated
calcium channels in the central nervous system)

IT Analgesics
Anticonvulsants
Antihypertensives
Nervous system agents
(preparation of 1-amino-3,3-diphenylpropanes and related compds. as

noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT Brain, disease

(stroke, treatment; preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT 1140-29-0P 4361-43-7P 4646-55-3P 5341-16-2P 5415-80-5P
5586-73-2P 5666-18-2P 17349-94-9P 19841-73-7P 28075-29-8P
36765-74-9P 48166-95-6P 53179-07-0P 64630-52-0P 90531-05-8P
91472-94-5P 95956-62-0P 98383-47-2P 98383-56-3P 106359-50-6P
118468-16-9P 144451-90-1P 144451-98-9P 144452-04-0P 144452-11-9P
159149-65-2P 170018-54-9P 170018-55-0P 170018-56-1P 170018-57-2P
170018-63-0P 170018-66-3P 170018-67-4P 170018-68-5P 170018-71-0P
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170018-77-6P 170018-78-7P 170018-79-8P 170018-80-1P 170018-81-2P
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186495-41-0P 186495-42-1P 186495-43-2P 186495-44-3P 186495-45-4P
186495-46-5P 186495-47-6P 186495-48-7P **186495-49-8P**
186495-50-1P 186495-51-2P 186495-52-3P 186495-53-4P 186495-54-5P
186495-55-6P **186495-56-7P** 186495-57-8P 186495-58-9P
186495-59-0P 186495-60-3P 186495-61-4P 186495-62-5P 186495-63-6P
186495-64-7P 186495-65-8P 186495-66-9P 186495-67-0P 186495-68-1P
186495-69-2P 186495-70-5P 186495-71-6P 186495-72-7P 186495-73-8P
186495-74-9P 186495-75-0P 186495-76-1P 186495-77-2P 186495-78-3P
186495-79-4P 186495-80-7P 186495-81-8P 186495-82-9P 186495-83-0P
186495-84-1P 186495-85-2P 186495-86-3P 186495-87-4P 186495-88-5P
186495-89-6P 186495-90-9P 186495-91-0P 186495-92-1P 186495-93-2P
186495-94-3P 186495-95-4P 186495-97-6P 186495-98-7P
186495-99-8P 186496-00-4P 186496-01-5P 186496-02-6P
186496-03-7P 186496-04-8P 186496-05-9P 186496-06-0P 186496-07-1P
186496-08-2P 186496-09-3P 186496-10-6P 186496-11-7P 186496-12-8P
186496-13-9P 186496-14-0P 186496-15-1P 186496-16-2P 186496-17-3P
186496-18-4P 186496-19-5P 186496-20-8P 186496-21-9P 186496-22-0P
186496-23-1P 186496-24-2P 186496-25-3P 186496-26-4P 186496-27-5P
186496-29-7P 186496-30-0P 186496-71-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT 75-16-1, Methylmagnesium bromide 95-46-5, 2-Methylbromobenzene
103-67-3, N-Benzylmethylamine 105-34-0, Methyl cyanoacetate 135-02-4,
2-Methoxybenzaldehyde 140-88-5, Ethyl acrylate 285-67-6, Cyclopentene
oxide 345-70-0, 3,3'-Difluorobenzophenone 372-20-3, 3-Fluorophenol
452-08-4, 2-Bromo-4-fluoroanisole 456-48-4, 3-Fluorobenzaldehyde
529-20-4, 2-Methylbenzaldehyde 578-57-4, 2-Bromoanisole 587-04-2,
3-Chlorobenzaldehyde 867-13-0, Triethyl phosphonoacetate 1073-06-9,
3-Fluorobromobenzene 2627-86-3, (S)- α -Methylbenzylamine
20595-30-6, trans-3-Fluorocinnamic acid 21900-39-0, 5-Fluoro-2-
methylbenzoyl chloride 65416-24-2, Benzyl crotonate 77532-79-7,
5-Fluoro-2-methylbenzonitrile 147624-13-3, 3-Fluoro-2-methylbenzaldehyde
170019-09-7 186496-59-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

IT 455-67-4P 458-45-7P 701-38-2P 1018-97-9P 2537-48-6P, Diethyl
cyanomethylphosphonate 2845-91-2P 17480-69-2P 25772-94-5P
38158-77-9P 75762-57-1P 84648-43-1P 98586-06-2P 98586-21-1P
156868-83-6P 170019-11-1P 170019-12-2P 170019-13-3P 170019-14-4P
170019-15-5P 170019-17-7P 170019-18-8P 170019-19-9P 170019-20-2P
186496-31-1P 186496-32-2P 186496-33-3P 186496-34-4P 186496-35-5P
186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P 186496-40-2P
186496-41-3P 186496-42-4P 186496-43-5P 186496-44-6P 186496-45-7P
186496-46-8P 186496-47-9P 186496-48-0P 186496-49-1P 186496-50-4P
186496-51-5P 186496-52-6P 186496-53-7P 186496-54-8P 186496-55-9P
186496-56-0P 186496-57-1P 186496-58-2P 186496-60-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 1-amino-3,3-diphenylpropanes and related compds. as noncompetitive antagonists of glutamate receptor operated calcium channels in the central nervous system)

L5 ANSWER 27 OF 27 USPATFULL on STN

ACCESSION NUMBER: 96:72128 USPATFULL

TITLE: Universal, hydraulic, self adjusting, work clamping device

INVENTOR(S): Schuit, Johannes, 1433 Camilo Trillado, Carpinteria, CA, United States 93013

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 5544872 | | 19960813 |
| APPLICATION INFO.: | US 1994-288688 | | 19940811 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Watson, Robert C. | | |
| LEGAL REPRESENTATIVE: | Haefliger, William W. | | |
| NUMBER OF CLAIMS: | 9 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 10 Drawing Figure(s); 4 Drawing Page(s) | | |
| LINE COUNT: | 256 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Apparatus for clamping and orienting work relative to a tool, for processing, comprising, in combination two laterally extending longitudinally separated support bars, and connector means connected to and extending between the bars for positioning them in fixed separated condition, there being work receiving space between the bars; bar leveling means extending downwardly from the bars for supporting the bars on a support bed, the means being adjustable to adjust the leveling of the bars; and work clamping pistons carried by the bars for hydraulically actuated movement toward the work receiving space for engaging and clamping the work to hold the work in fixed position relative to the bed.

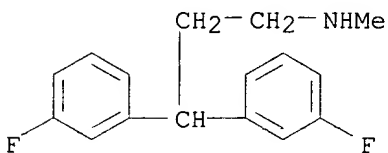
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 186495-49-8P 186495-56-7P 186495-99-8P
273409-53-3P

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

RN 186495-49-8 USPATFULL

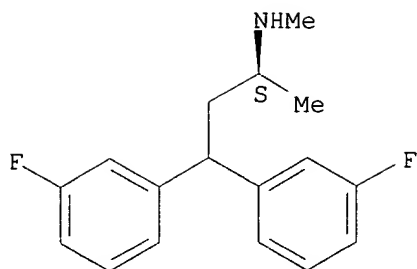
CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



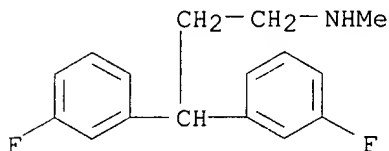
RN 186495-56-7 USPATFULL

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

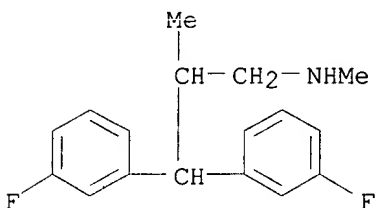


RN 186495-99-8 USPATFULL
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
 hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 273409-53-3 USPATFULL
 CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N,β-dimethyl-,
 (9CI) (CA INDEX NAME)



IT Ionophores
 (NMDA receptor complex; preparation of aralkylamines active at
 receptor-operated calcium channels as neuroprotectants)

IT Glutamate receptors
 (NMDA-binding, ionophore complex; preparation of aralkylamines active at
 receptor-operated calcium channels as neuroprotectants)

IT Nervous system
 (degeneration, treatment; preparation of aralkylamines active at
 receptor-operated calcium channels as neuroprotectants)

IT Cytoprotective agents
 (neuroprotectants; preparation of aralkylamines active at receptor-operated
 calcium channels as neuroprotectants)

IT Calcium channel
 (preparation of aralkylamines active at receptor-operated calcium channels
 as neuroprotectants)

IT 5586-73-2P 28075-29-8P 90531-05-8P 133805-32-0P 144451-98-9P
 144452-04-0P 144576-90-9P 148920-48-3P 170018-48-1P 170018-49-2P
 170018-50-5P 170018-51-6P 170018-52-7P 170018-54-9P 170018-55-0P
 170018-56-1P 170018-57-2P 170018-63-0P 170018-66-3P 170018-67-4P
 170018-68-5P 170018-71-0P 170018-72-1P 170018-73-2P 170018-74-3P
 170018-75-4P 170018-76-5P 170018-77-6P 170018-78-7P 170018-79-8P
 170018-80-1P 170018-81-2P 170018-82-3P 170018-83-4P 170018-84-5P
 170018-85-6P 170018-86-7P 170019-10-0P 186495-37-4P 186495-38-5P
 186495-39-6P 186495-40-9P 186495-41-0P 186495-43-2P 186495-44-3P
 186495-45-4P 186495-46-5P 186495-47-6P 186495-48-7P

186495-49-8P 186495-50-1P 186495-51-2P 186495-53-4P
 186495-54-5P **186495-56-7P** 186495-93-2P 186495-94-3P
 186495-95-4P 186495-97-6P 186495-98-7P **186495-99-8P**
 186496-00-4P 186496-02-6P 186496-03-7P 200430-18-8P 217658-89-4P
 217658-94-1P 217658-96-3P 217659-01-3P 217659-23-9P 217660-61-2P
 273409-48-6P 273409-49-7P 273409-50-0P 273409-51-1P 273409-52-2P
273409-53-3P

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 62-23-7, p-Nitrobenzoic acid 85-41-6, Phthalimide 100-52-7,
 Benzaldehyde, reactions 105-34-0, Methyl cyanoacetate 107-13-1,
 2-Propenenitrile, reactions 109-76-2, 1,3-Diaminopropane 110-60-1,
 1,4-Diaminobutane 135-02-4, o-Anisaldehyde 285-67-6, Cyclopentene
 oxide 345-70-0, 3,3'-Difluorobenzophenone 443-73-2,
 5-Fluoroindole-3-acetic acid 452-08-4, 2-Bromo-4-fluoroanisole
 456-48-4, 3-Fluorobenzaldehyde 462-94-2, 1,5-Diaminopentane 529-20-4,
 2-Methylbenzaldehyde 546-68-9 578-57-4, 2-Bromoanisole 587-04-2,
 3-Chlorobenzaldehyde 932-31-0, 2-Methylphenylmagnesium bromide
 1073-06-9, 1-Bromo-3-fluorobenzene 4587-33-1 5003-71-4 5460-29-7,
 N-(3-Bromopropyl)phthalimide 7300-34-7, 4,9-Dioxa-1,12-dodecandiamine
 17318-03-5, 3-Fluorophenylmagnesium bromide 17480-69-2,
 (S)-N-Benzyl- α -methylbenzylamine 50715-13-4 65416-24-2, Benzyl
 crotonate 77532-79-7, 5-Fluoro-2-methylbenzonitrile 122630-41-5
 147624-13-3, 3-Fluoro-2-methylbenzaldehyde 168080-76-0,
 3-Fluoro-2-methylbenzoyl chloride 263355-05-1, 3-Fluoro-2-
 methylphenylmagnesium bromide

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT 455-67-4P 701-38-2P 4748-73-6P 14209-32-6P 35513-93-0P
 38158-77-9P 51644-96-3P 75762-57-1P 83948-53-2P 98586-06-2P
 101187-29-5P 114459-62-0P 122248-82-2P 122631-98-5P 122632-01-3P
 122632-02-4P 128550-02-7P 128550-03-8P 128550-05-0P 128550-06-1P
 128550-07-2P 144923-52-4P 147875-12-5P 147875-14-7P 170018-87-8P
 170018-88-9P 170018-89-0P 170018-90-3P 170018-92-5P 170018-96-9P
 170018-97-0P 170019-07-5P 170019-09-7P 170019-11-1P 170019-14-4P
 170019-15-5P 170019-16-6P 170019-17-7P 170019-18-8P 170019-19-9P
 170019-20-2P 170019-21-3P 170019-22-4P 170019-23-5P 170019-24-6P
 170019-25-7P 186496-31-1P 186496-32-2P 186496-33-3P 186496-34-4P
 186496-35-5P 186496-36-6P 186496-37-7P 186496-38-8P 186496-39-9P
 186496-40-2P 186496-41-3P 186496-42-4P 186496-44-6P 186496-45-7P
 186496-46-8P 186496-48-0P 186496-51-5P 186496-52-6P 186496-53-7P
 273409-54-4P 273409-55-5P 273409-56-6P 273409-57-7P 273409-58-8P
 273409-62-4P

(preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)